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The Single Convention on narcotic drugs and the prevention of drug addiction

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A. INTRODUCTION : CHINA'S PART IN THE INTERNATIONAL CONTROL OF NARCOTIC DRUGS

The international control of narcotic drugs, which has been in force for nearly half a century, came into being partly as a result of international efforts to cope with China's opium problem; the initial regime of control was closely related to the suppression of opium-smoking in China. It is significant that out of nine resolutions adopted by the first meeting of the International Opium Commission held at Shanghai in 1909 under the sponsorship of the United States Government, five dealt with the opium situation in China. The 1912 Hague Convention devoted a whole chapter — namely, chapter IV — to control measures in regard to the opium traffic and addiction within Chinese territories. Information relating to the application of these measures was regulary reviewed by the competent international control agency on the basis of annual reports submitted by the governments concerned. This practice was discontinued only a few years ago, when such information was no longer required under the revised standard form for annual reports.

Progress made in China has had far-reaching effects on the international control of narcotic drugs throughout the world, for the Chinese people and Government have not only undertaken internal measures of control, but have also shown a deep interest in the development of an international regime of control and made constructive proposals towards this end. Since 1909, a growing number of anti-narcotics organizations have been set up by the Chinese people in order to call upon the Government to pursue a firm and positive policy of control, and to participate directly in international activities aimed at the suppression of the abuse of narcotics. Thus, for example, there was established in October 1910, at Peiping, a Chinese National Anti-narcotics Association whose main objective was to bring about the abrogation of opium treaties concluded between China and other countries concerned and to hasten the completion of a domestic control programme. In 1918, a universal association for the suppression of the abuse of opium was organized to promote control measures on both national and international levels. Its activities in the international field included (i) urging, by telegram, the Versailles Peace Conference to incorporate provisions regarding narcotics control in the peace treaties; (ii) requesting the Universal Postal Union to prohibit the mailing of narcotic drugs; and (iii) seeking the co-operation of diplomatic representatives accredited to China, and other foreign nationals, in the implementation of international control measures. Later, in anticipation of the International Opium Conference about to be convened at Geneva in November 1924, a Chinese National Narcotics Suppression Association was formed as an expression of the Chinese people's enthusiastic support for the international co-operative efforts. It transmitted to the conference an appeal calling for the adoption of strict measures of control and the limitation of the production of narcotics to meet medical and scientific needs. The appeal was signed by more than 4,200 civic bodies, representing a total membership of about 4,663,000 persons.

With regard to the policy of the Chinese Government, a firm basis was laid down in 1924 by Dr. Sun Yat-sen, founder of the Republic, when, on the occasion of his assumption of the office of the Commander-in-Chief of the National Government, he declared: "The public opinion of the Chinese people, especially of law-abiding and respectable citizens, is against the abuse of opium. Any attempt to legalize the opium traffic or to appease the evil forces of opium, however expedient it may seem to be, is contrary to the public interest. ... Our campaign against opium admits of no compromise and should never be given up. If any government authority seeks a truce in this campaign in order to promote its selfish and short-sighted interest, it should be regarded as committing an act of treason." Unfortunately, this policy could not be immediately carried into effects, as China was not yet unified at that time.

As soon as unification was achieved by the National Government in 1927, following the successful Northern Expedition, Generalissimo Chiang Kai-shek proclaimed the suppression of the abuse of opium as one of the primary tasks in the administrative programme. Time after time he reminded the Chinese people that the fulfilment of this task was an essential step towards administrative reform and national reconstruction. In his opinion, determined efforts must be made to blot out the evil of opium which had plagued China for more then a century. At the height of the governmental campaign against opium, the Generalissimo himself took over the post of Director-General of the Suppression of the Abuse of Opium and drew up a plan for suppression by stages. The basic objectives, as stated in one of the major legislative measures enacted at that period, were to carry out international obligations in respect of the control of narcotic drugs and to bring about the abolition of the abuse of narcotic drugs in China.

The Chinese Government pursued these objectives even when faced with extreme difficulties in the course of the Sino-Japanese war. As a matter of fact, Generalissimo Chiang declared during the war: " The campaign against opium is no less important than the war of national resistance; they should be prosecuted with equal vigour." Thanks to these unremitting efforts, the centuries-old scourge of opium was gradually eliminated in China.

By the end of World War II, the Chinese Government was confronted with the problem of curing and rehabilitating numerous drug addicts living in areas formerly under Japanese occupation. It also had to maintain effective measures of control in the rest of the country in order to prevent a revival of drug addiction. To deal with these post-war problems, the Government appointed Mr. Wang Te-pu, the present Minister of the Interior, to be chairman of the National Narcotics Suppression Commission. During the war, Mr. Wang, as director of the Department of Civil Affairs of the Shensi province, had distinguished himself in his service in connexion with the suppression of the abuse of narcotic drugs. As chairman of the National Commission, he paid equal attention to domestic measures of control and to international co-operation. His internal policy consisted in " using patient persuasion before applying stern penalties, and giving first priority to the prohibition of drug addiction ". Internationally, he called for close co-operation with governements of friendly nations in the implementation of the existing international conventions, as well as in the adoption of more effective measures of control. In his opinion, the world production of opium far exceeded the legitimate needs; it was therefore imperative that the principal opium-producing and opium-consuming countries should meet to negotiate an agreement to limit the cultivation of the opium poppy and to put the supply of raw opium under strict control, so that the illicit traffic in opium and its preparations might be suppressed. His views were embodied in a proposal submitted by the Chinese delegation to the third session of the Commission on Narcotic Drugs. After adoption by the Commission, the proposal formed the basis of resolution 159 E (VII) of the Economic and Social Council, thus paving the way for the convening of the United Nations Opium Conference in 1953.

B. PENALTIES FOR DRUG ADDICTION

Within the system of international control, every kind of illicit activity relating to narcotic drugs, whether it be addiction, cultivation, transport, selling, manufacture or possession of drugs, should be made a punishable offence by national legislation. To leave any of them free from legal sanction is to create a loophole in the whole system liable to reduce the effectiveness of international control. However, a study of the existing international conventions shows that while they generally condemn narcotics offences, they contain no provisions on penalties for drug addiction. Their silence on that subject is presumably due to the following considerations:

(*a*) Drug addicts are in some cases found to have acquired the habit through using drugs as sedative or curative medicine. They are more to be pitied than condemned. Therefore, to punish them seems undesirable on humanitarian grounds.

(*b*) Drug addicts are all victims of illicit traffickers. It is the latter that should be subject to severe punishment. Once the sources of supply were cut off, there would be no problem of drug addiction.

(*c*) In view of the wide divergencies in the policy and practice followed by various governments with regard to the problem of drug addiction, it seems inadvisable for an international convention to impose a uniform obligation of adopting punitive measures against drug addicts. Such a convention would probably be unacceptable to some states and would be acceptable to others with misgivings. In any case, the effectiveness of the convention would be reduced.

(*d*) Drug addiction is a matter of domestic concern, and has no international significance. The problem of whether it should be outlawed is for each country to decide and has no place in an international convention which is mainly designed to co-ordinate governmental efforts in the suppression of illicit traffic.

The proposed single convention follows the pattern of the existing international agreements in that it makes no provisions on the penalty for drug addiction. It merely states in article 50, chapter X, that the parties should use their best endeavours to secure the compulsory treatment of drug addicts with a view to restoring their health. By laying emphasis on the rehabilitation aspect of the problem rather than on the prevention, it shows a more lenient attitude towards addicts than the policy of punishment followed by certain countries. In our view, the whole approach calls for a thorough re-examination in which the following factors must be taken into account:

1. *The Causes of Addiction*

While the causes of addiction are many and varied, drug addicts may be classified into two or three categories. Several years ago, Mr. Garland H. Williams, District Supervisor of the United States Bureau of Narcotics, in an article entitled " The Narcotic Addiction Problem and a Suggested Solution ", referred to two types of drug addict, as follows:

" The *medical addict*, who is sick and under the professional care of a physician who has properly determined that narcotic drugs are medicinally required in the treatment of the disease. Such an addict secures drugs without difficulty."

and

" The *criminal addict*, who has no recognized medical need for narcotics and takes the drug only to satisfy his destructive craving, and in order to carry on his criminal activities."

At the first session of the Commission on Narcotic Drugs, Dr. Jorge A. Lazarte, the representative of Peru, classified addicts into three groups — namely, incidental addicts with a well-balanced personality who acquire the habit as result of improper medical management, and who are generally easily cured; psychoneurotic addicts who resort to the use of drugs to obtain relaxation; and psychopathic addicts who exhibit definite asocial and amoral behaviour and who generally have a criminal background. Among these three groups, cases of the first two can easily be prevented without recourse to punitive measures.

In China as well as in other countries, drug addiction attributable to medical treatment is not regarded as a punishable offence. It must be pointed out, however, that with the discovery by modern medical science of effective substitutes for narcotic drugs in the treatment of diseases, the possibility of acquiring the habit through medical dosage is becoming smaller. Furthermore, as the use and supply of narcotics for therapeutic purposes are nowadays placed under strict control in almost every country, a patient can have access to the drugs only by his physician's order and prescription. This also helps to reduce the number of medical addicts. According to our information, in recent years over 90% of addicts are found to have acquired the habit not as a result of improper medical treatment, but because of their abnormal and inexcusable craving.

Since drug addiction is liable to inflict bodily harm on the addict, it is certainly a matter of concern to the community. Legal sanction should therefore be provided as a matter of national and social policy. In a sense, drug addiction is a social offence comparable to an attempt to commit suicide, which is punishable by law in certain countries. Penalty for drug addiction is further justified by the fact that it is invariably associated with other criminal activities. As Mr. Harry J. Anslinger, United States Commissioner of Narcotics, pointed out in his book entitled *The Traffic in Narcotics*,

" A spot check of any police record bureau will disclose the fact that many addicts were criminal offenders long before taking on the drug habit. Make no mistake about it. . . . We are not dealing with something hospitalization alone will cure, but a dreaded scourge that penetrates infinitely deeper and requires a much greater effort to uproot."

While some addicts have previous police records, others become criminal after acquiring the drug habit. An addict lives in mental disorder and will stop at nothing to get the drug to satisfy his craving. His shameful way of life poses a threat to social order and good morals. According to a recent report released by the Metropolitan Police Board of Tokyo, some 70% of juvenile delinquents in Japan are addicted to " hiropon ", a strong, stimulating and habit-forming drug (*Nippon Times*, 18 August 1953). Official reports published in various countries have also definitely established the link between the use of marihuana and crime. The criminal character of drug addiction also lies in the fact that addiction spreads from one person to another like an infectious disease. The Commission on Narcotic Drugs has given increasing attention to this problem of contamination and urged member states to take effective measures of prevention. At its tenth session, the Commission requested the secretariat to study the problem of drug addiction in conjunction with the problem of crime prevention, and called the attention of the Social Commission to the relationship between these two problems. All this clearly shows that drug addiction, far from being a personal problem, is generally regarded as a curse to the world community.

For the reasons stated above, a large number of states have come to regard the abuse of drugs as a punishable offence. There is also a tendency to impose heavier penalties for it. Mr. Anslinger, United States Commissioner of Narcotics, in advocating stringent punishment for drug addicts, wrote in his book quoted above:

" Strong law, good enforcement, stiff sentence and a proper hospitalization program are the necessary foundations upon which any successful program must be predicated. These, plus an alert and determined public, will go a long way toward blotting out the problem. Probably the greatest reason for an increase in drug addiction has been the failure on the part of the legislators, or police and of other officials to observe these important fundamentals."

It may be recalled that, at the first session of the Commission on Narcotic Drugs, Mr. Nasroah Entezam, the representative of Iran, stated that a bill then before the Iranian Parliament included a paragraph providing for the death penalty for any one found smoking opium. A recent report of the Commission indicates that during its twelfth session " several representatives urged that criminal addicts should receive longer prison sentences and that other addicts should be forced to undergo as long a period of medical treatment as was necessary to complete their rehabilitation ". According to the same report, " in Egypt, in China and in the United States, experience had shown the effectiveness of long prison sentences, and the possibility of giving longer sentences was under consideration in India ". The report further points out that " while representatives were generally in favour of the treatment measures proposed by the study group of the World Health Organization, they nevertheless felt that addicts, particularly criminal addicts, could not always be treated solely on a medical and not on a punitive basis".

Criminal addicts have always been liable to punishment under Chinese law. As early as 1813, the eighteenth year of the reign of Emperor Chia Ching of the Ching Dynasty, a set of regulations governing the penalties for opium-smoking was promulgated. This was followed in 1839, the nineteenth year of the reign of Emperor Tao Kwang, by another set of regulations consisting of thirty-nine articles. Article 14 of the new regulations provided: " All opium addicts must rid themselves of the habit within a period of one year and six months. Any person, whether a governmental official or an ordinary citizen, who fails to do so shall be liable to the death penalty." As a result, most addicts submitted themselves to a cure, and it appeared then that the evil of opium-smoking would be brought under control. Unfor-

tunately, diplomatic setbacks suffered by the Manchu Government in the next few decades led to an upsurge of drug addiction in China.

Since the establishment of the Republic of China, penalties for drug addicts have varied in severity in accordance with the over-all suppression programmes adopted by the Government at various stages. In 1940, when the target date for gradual suppression of the abuse of narcotics was reached, the Government decided to increase penalties for drug addiction to strengthen its policy of total prohibition. For this purpose, special regulations were promulgated to supersede the section in the Penal Code dealing with opium offences. Under these regulations, the first offence in the case of drug addiction is punishable by imprisonment of from one to five years, and the second offence by life imprisonment or the death penalty; heavier penalties may be imposed on government employees convicted of addiction. Mr. Wang Te-pu, at that time director of the Civil Affairs Department of the Shensi province, was convinced that, to carry out the policy of total prohibition, public opinion must be mobilized to denounce narcotics offenders, and law-enforcement agencies must undertake the prosecution of narcotics cases without fear or favour. He therefore announced various measures to encourage the general public to inform on drug addicts. To set an example, he himself brought a charge of opium-smoking against one Tang Chi-ling, president of the Higher Court of the Shensi province. These measures were so successful that within a few years narcotic addiction was stamped out in the whole Shensi province with the exception of its northern part, which, under the control of Chinese Communists, remained a base for the illicit cultivation of and traffic in opium and other narcotic drugs.

After World War II, the Chinese Government attached even more importance to punitive measures against drug addicts in pursuance of its policy of " placing special emphasis on the prohibition of addiction ". In enforcing penalties already provided by law, it sought first to persuade addicts, by means of education and publicity, to give up the habit voluntarily. Those who failed to do so within a specified time limit were subject to punishment in accordance with the law. This method proved most effective. Later, in 1955, the Chinese Government enacted the " Regulations for the Suppression of the Abuse of Opium and other Narcotic Drugs in the Period of National Emergency " in order to check narcotics-smuggling activities carried on by Chinese Communists. While following the general policy of " using patient persuasion before applying stern penalty ", the new regulations increased penalties for drug addiction by providing imprisonment of from three to seven years for the first offence, imprisonment of a term equivalent to one and two-thirds of the original sentence for the second offence, and life imprisonment or the death penalty for the third offence. These regulations have also proved to be very effective.

2. *The Root of the Narcotics Evil*

At the end of World War II, the Chinese Government was determined to suppress as soon as possible the abuse of narcotic drugs in areas formerly under Japanese occupation. Mr. Wang Te-pu, who was then in charge of the national narcotics administration, believed that the best way to do this was to place special emphasis on the prohibition of drug addiction. He said: " Special attention must be given to the prohibition of drug addiction, which is the root of the narcotics evil. Narcotics can be a blessing if used properly for therapeutic purposes. They become harmful only when people are addicted to them. If there were no addicts, narcotics would not be sold at such high prices as to induce profit-seekers to engage in the illicit traffic. Furthermore, illicit traffickers, once they have repented, can easily renounce their unlawful activities. It is much more difficult for addicts to obtain a complete cure, because they are physically and mentally under the influence of the drugs, which takes a considerable length of time to overcome. From the administrative point of view, once the prohibition of addiction is successfully carried out, illicit traffickers would be out of business, and the problem of illicit traffic would be solved by itself. The prohibition of drug addiction is indeed the key to the solution of the whole problem. Therein lies our primary task." To carry out this programme, he sent inspectors to the areas concerned to check the progress of the prohibition work. As a result, within a set period of two years, drug addiction was brought under control.

The Commission on Narcotic Drugs now has at its disposal a number of excellent studies made by United States and Canadian experts on the subject of the cure of addiction. The Division of Narcotic Drugs of the United Nations Secretariat has also given increasing attention to the work of conducting surveys and preparing reports in the field of drug addiction. Its has made available to the Commission some analytical studies of the information on drug addiction supplied by governments. These documents are of great value to member states in their work of combating drug addiction. As was rightly observed at the eleventh session of the Commission, the problem of drug addiction provided the touchstone for all the others, and for the Commission's work as a whole. Mr. Panopoulos, the representative of Greece, pointed out at the same session that the Commission could not afford to neglect this problem, since its ultimate objective was to abolish addiction throughout the world. Earlier, at the ninth session of the Commission, Dr. H. R. Wei, the representative of China, commenting on the draft of a model code for the application of the 1953 Opium Protocol, stressed that the reference to opium-smoking in annex II C (C) of the draft code should be interpreted in the spirit of resolution X of the 1953 Opium Conference, which underlined the obligation of all parties to the Protocol to suppress opium-smoking with the least possible delay. All these statements reflect a general concern over the need of suppressing drug addiction.

It may be argued that since the entire system of control is designed to attain the ultimate objective of eliminating addiction through suppression of the illicit cultivation and manufacture of and traffic in drugs, it is not necessary to place emphasis on the prohibition of addiction. Although this argument appears to be logical, past experiences neverthe-

less show that a control policy which seeks to eliminate addiction by the devious means of controlling the sources of supply without an outright prohibition of addiction is of little practical value. As long as the supply of drugs to addicts can yield huge profit, the illicit market will flourish. At the third session of the Commission on Narcotic Drugs, Col. C. H. L. Sharman, the representative of Canada, pointed out that the disparity of prices on the illicit market was largely responsible for encouraging the traffic. As an illustration, he mentioned that opium which was sold for ten dollars a pound in Bombay fetched 600 to 900 dollars a pound in North America. It is no wonder, therefore, that illicit traffickers have no scruples about violating the law by using modern transportation and communication facilities to engage in smuggling activities. According to an estimate made by the Advisory Committee on Opium and other Dangerous Drugs of the League of Nations, the amount of drugs seized represented no more than 10% of the total volume of the illicit traffic. The situation at present would seem to be about the same, as can be seen from the following findings of the Commission on Narcotic Drugs:

(*a*) On the illicit traffic in raw opium, the tenth session of the Commission noted that, as in the past, it seemed to be concentrated in the Middle and the Far East during 1954. As far as its extent was concerned, it would seem that " the traffic was now at about the same level as twenty-five years ago ". The Commission also observed in the report on its eleventh session that the figures of seizures showed " no apparent decline in the traffic in opium ". " During the past five years the raw opium seizures had averaged approximately 48,000 kg. per year; the 1955 figure, 49,100 kg, though incomplete, had already exceeded this average and could be expected to be still higher."

(*b*) As regards morphine, the Commission, at its tenth and eleventh sessions, noted that there was an increasing tendency for conversion into morphine to take place near the area of cultivation of the opium poppy.

(*c*) On the illicit traffic in heroin, the Commission, at its eleventh session, observed that the traffic was still going on on a large scale. The 1955 figure of seizures — 143 kg 486 gr — though incomplete, had already increased by about one-third in comparison with 1954.

(*d*) At its eleventh session, the Commission also noted that the ingenuity of smugglers regarding concealment of drugs appeared to be limitless, and expressed its sympathy with the extremely difficult task of national preventive services.

In view of these facts, one cannot but agree with the following remarks made by the representative of Turkey at the twelfth session of the Commission:

" In order effectively to combat the illicit traffic, it was not enough to concentrate on origins — the problem must be studied as a whole from a wider point of view. ... Attention must therefore be paid to the other related aspects of the question — namely, on the one hand to the control system prevailing in the countries of transit, particularly at the frontiers, and, on the other, to the attraction offered by the consumer market, which encourages traffickers to cross frontiers. The question had three integral phases, and if both legislative and administrative measures were not applied with the same degree of severity in all three, there would always be a flow of traffic."

3. *The Basic Purpose of an International Narcotics Convention*

An international narcotics convention is designed to ensure the elimination of the abuse of narcotic drugs in the interest of the health and well-being of mankind. It is based on humanitarian principles, rather than on national interests, as in the case of international treaties of a political and economic nature. Therefore, in drawing up such a convention, paramount consideration should be given to the most effective ways to attain the noble objective. To the extent compatible with the principles of international law, the convention should provide for strict measures to meet actual needs. This is especially true with regard to the prohibition of drug addiction, for the reason that after World War II most countries in the Far East have given up the system of state monopolies for opium and that there is already a general trend towards making drug addiction a punishable offence. The time has come for the proposed Single Convention to make more drastic provisions on this subject than the existing conventions. While such provisions may be at variance with the position taken by a few countries, it is hoped that the latter will still find it possible to accept the convention in the interest of the world community, or, in case of absolute necessity, to accept it with reservations. In this connexion, one cannot but admire a statement made by Mr. Vaille, the representative of France, at the eleventh session of the Commission on Narcotic Drugs, which gave full expression to the spirit of compromise. Commenting on the " clause on inquiry " in the 1953 Opium Protocol, he said: " Even if the protocol had contained a mandatory clause on inquiry which some countries regarded as an infringement of their national sovereignty, the French Government would no doubt have accepted it, although there was no drug addiction or opium production problem in France. It would have done so in a spirit of international solidarity, which should be the basis of all the work carried out by the United Nations in the narcotic field."

Furthermore, as the proposed convention is concerned with the welfare of mankind, its success depends not only on faithful observance of their obligations by the governments concerned, but also on the understanding and support of the peoples throughout the world. The abuse of drugs has caused great harm to the international community. Drug addiction is abhorred by good citizens everywhere. If punishment for addiction were made mandatory under the proposed convention, the general public would surely support the measure and help their governments to enforce it. This would ensure the success of the convention. On the other hand, if the convention did not provide penalties for drug addiction, it would disappoint the peoples of the world and invite public criticism. It might even adversely affect the work of narcotics control in certain countries. For in countries where addiction is punishable by law, enforcement of the penalty would be made difficult by the fact that their

national legislation does not accord with the provisions of international convention. In countries where addiction is not punishable by law, the fact that the convention does not provide any guidance in this respect would make its observance a matter of formality.

4. *The Protection of Nationals residing abroad*

There is yet another important reason why provisions should be made in the proposed convention requiring the parties to adopt the necessary legislative measures to render drug addiction a punishable offence. That is that such provisions would enable a state which finds any of its nationals residing in another state addicted to narcotic drugs to call upon the state of residence to take appropriate measures of prohibition. Under present circumstances, a state can enforce the prohibition of addiction only within its territorial jurisdiction; it can do nothing about its nationals residing abroad who are drug addicts, if drug addiction does not constitute a punishable offence under the national legislation of the state of residence. The only remedy is to include in the proposed convention a suitable clause whereby each party would undertake to adopt the necessary measures to render drug addiction punishable under its domestic laws. Such a clause would serve to protect the welfare of all persons, regardless of their place of residence, and is in conformity with the interest of humanity.

During the second Geneva Opium Conference, held in 1925, the Chinese National Association for the Suppression of the Abuse of Opium sent to the conference a strong appeal on the question of drug addiction among overseas Chinese. It was stated that in view of the undeniable fact that a large number of Chinese nationals residing in the colonial territories of western Powers, such as the Straits Settlements and the Dutch East Indies, were addicted to opium and other dangerous drugs, the governments concerned should enter into an agreement with a view to taking effective joint action to put an end to this situation. Acting on popular demand, the Chinese Government also instructed its delegation to call upon the western Powers to take preventive measures within their colonial territories. As the conference failed to comply with this request, the Chinese delegation withdrew from the conference. In a statement explaining the reason for its withdrawal, the Chinese delegation made clear that it could not accept any proposal that did not give definite assurance that the legalized trade in prepared opium would be brought to an end within a reasonable period of time, as suggested by the Chinese delegation. At about the same time, the United States delegation also withdrew from the conference on the instructions of its government because of the failure of the conference to adopt its proposal regarding the limitation of the production and supply of opium.

Now that most countries have given up the system of state monopolies for opium, the problem of drug addiction among overseas Chinese is becoming less and less serious. However, the Chinese Government is still deeply concerned with occasional reports in recent years about the abuse of drugs among Chinese nationals residing in certain foreign territories. In the interest of protecting overseas Chinese from the evil of drugs, it seems to the Chinese Government all the more desirable that the proposed convention should require the parties to adopt strong measures of prohibition applicable to all persons, regardless of nationality, who reside within their territories.

C. PUBLICITY AND EDUCATION

Another weapon against the abuse of drugs is publicity and education, both of which should go hand-in-hand with legal sanction. In the present draft Single Convention, no new provision on publicity and education has been added. What is more, it does not even include the flexible provision of article VII of the 1925 Geneva Agreement, which reads: " The Contracting Powers shall use their utmost efforts by suitable instruction in the schools, dissemination of literature and otherwise, to discourage the use of prepared opium within their respective territories, except where a government considers such measures to be undesirable under the conditions existing in its territory."

The reason for this omission is probably the fear that under certain conditions publicity on the harmful effects of taking drugs may lead men to sample them out of curiosity and become addicts in the end. Far back in the days of the League of Nations, a resolution was adopted to call the attention of member states to this possible outcome. During the various sessions of the Commission on Narcotic Drugs, it has also been stressed that in countries where narcotic drugs are not a serious problem, publicity and education against their abuse can sometimes do more harm than good.

While we do not deny that the above point of view is to a certain extent valid, we must say that on the whole, publicity and education against the misuse of narcotics will reap far more benefits than evil effects, and they are necessary weapons to fight against addiction. If fear of ensuing evils at some time or in some localities prevents the inclusion of a stipulation to that effect in the Single Convention, it might be a case of " refraining from eating for fear of choking ", as the Chinese saying goes.

From the point of view of criminal jurisprudence, we find that criminal policy has changed with social evolution. Gradually, it has shifted from the traditional theory of retaliation to that of prevention. As we know, causes for the commission of crimes are closely related with the political and social conditions of the time. Modern criminal legislation therefore places emphasis on education and conversion of the criminals. The object lies more in the prevention of future offences than in the mere infliction of penalties for crimes already committed.

In the case of narcotic drugs, their harm and the stern measures of control are usually not clearly understood by the people. Therefore, in the administration of controls

we must first make use of education and persuasion for the dual purpose of reforming the offenders and preventing would-be offenders. An opportunity should be given to the offenders to reform, and it is only when they have failed to do so that they should be punished according to the law. This would be consistent with the modern concept of jurisprudence.

Basing itself on such concepts, the Chinese Government has included in all its narcotics laws a provision to the effect that, before an addict is sentenced, he is to be given a period of grace during which he is educated and admonished so that he may rid himself of drug addiction and free himself from his impending penalty. Only if he fails to reform during the period of grace is he punished according to the law. Experience has shown that this way of combating addiction works wonders.

Speaking at the tenth session of the Commission on Narcotic Drugs, Mr. J. H. Walker, the representative of the United Kingdom, said: " The public, and especially young persons, should be educated to consider opium addiction as a pernicious vice to be reprobated. That would go half way towards solving the problem. Many people in many countries do not at present consider opium or cannabis smoking as an evil." He illustrated his statement by referring to the temperance movement in the United Kingdom. The speaker should be commended for his well-founded statements.

As addiction is a social problem, to attack it by government action alone would be insufficient. To eliminate addiction completely, we must mobilize public opinion so as to change the attitude of the addict toward the use of narcotics, making him feel ashamed of what he is doing and voluntarily submit himself to medical treatment.

The most effective ways of arousing public opinion are publicity and education, which can show the people the harmful nature of narcotic drugs and induce them to wage anti-narcotic campaigns in support of government actions.

China's earliest anti-narcotics movement started in 1835 during the reign of Emperor Tao Kuang of the Ching Dynasty. The Government, in response to the deep concern shown by most enlightened people at that time at the growing evil of opium-smoking and to their suggestion of strict prohibition, took drastic steps to implement the prohibition policy. Later on, an anti-opium campaign was launched by the Christian community, and clinics were set up to give treatment to opium addicts. The press also gave wide publicity to the harm done by smoking opium and called for effective measures of control. In 1906, in the thirty-second year of Emperor Kuang Hsu's reign, the Government decided to prohibit opium-smoking, and enacted laws to enforce the decision. An Opium Suppression Bureau was established to take charge of control matters. At the same time, the people were encouraged to organize benevolent associations to assist the addicts, so as to help the Government carry out its prohibition policy. After that a mass movement against opium was started, and anti-drug societies such as the Chinese People's Opium Suppression Association, National Opium Suppression Association, Chinese Christian Anti-narcotic Committee and Chung Hwa Anti-narcotic Society were formed one after another. Of these organizations, Chung Hwa Anti-Narcotic Society's contribution to the control efforts is especially commendable. It presented to the Geneva Opium Conference the views of the Chinese people on the suppression of the abuse of opium. It also made many useful suggestions to the Government, such as the abolition of the public sale of opium.

The importance of public opinion may well be shown by the report to the Economic and Social Council on the work of the Permanent Central Opium Board in 1955: " In all countries, whether they be producers of raw materials, manufacturers or merely consumers of narcotic drugs, effective national control is the primary prerequisite for satisfactory fulfilment of the International Conventions. But each country has its own special problems, and these can only be solved with the continuing support of public opinion, on which the success of all efforts against the various forms of drug addiction ultimately depends."

Now I want to touch upon the contents of publicity. Publicity for the control of narcotics covers a wide area, from informing the people of the danger of narcotic drugs to all other matters related to the problem of drug addiction. When well conducted, publicity can produce excellent results and will not give rise to undesirable repercussions.

After World War II, the Chinese Government launched a publicity programme against narcotics for the purpose of teaching the people the harmful effect of narcotic drugs on people's health, their demoralizing influence, the serious drain they represent on the addict's finances, their harmful effect on the armed services and administrative personnel, and so on. In a handbook outlining the publicity programme, Mr. Wang Te-pu, in his capacity as Director of the Suppression of the Abuse of Opium, stated:

" The 'Outline of the Publicity Programme against Narcotics' contains details about the object and content of publicity, the history of opium suppression and the successes and failures of the movement, the principle and effectiveness of the measures now in use, and the ways and means of making publicity. All those who are engaged in opium suppression work should bear all these in mind and use them to advantage. However, in order to be effective, we must pay particular attention to the substance and technique of publicity.

" (1) *The Object of Publicity*. — In order to make the people fully understand why addiction must be abolished, we must acquaint them with the history of opium suppression — Dr. Sun Yat-sen's admonition against opium, the principal ideas of President Chiang Kai-shek's directions for carrying out opium-suppression campaigns, the teachings of Lin Tse-hsu concerning the abolition of opium-smoking, the spirit of the present government 's abolition policy, the actual condition of narcotics control at home and abroad, the principles of all the narcotics control laws, etc. We must make the non-addicts firmer than ever in their opposition to narcotics, and the addicts resolve to reform themselves.

" (2) *Publicity Technique*. — Publicity technique should vary with time, place, people and conditions. Sometimes, we change from direct inculcation to indirect references; sometimes we ask rehabilitated addicts to relate their experiences. Sometimes we use concrete facts to serve the purpose of publicity; sometimes

we use illustrated materials, always keeping in view our paramount objective of making people desist from taking drugs.

" (3) *Publicity and Locality.* — The manner of conducting a publicity campaign at the national level varies from that at the international level; so does the form of publicity in the interior provinces from that in the newly recovered territories. In enlightened areas or in ill-informed places, in opium-producing areas or in non-producing areas, all activities trying to mould public understanding should take into consideration local circumstances while observing strictly appropriate national laws and regulations and international conventions."

We are still actively carrying out this publicity programme, with some adjustments to suit the actual conditions of the present stage.

D. CONCLUSIONS

In conclusion, I wish to say that drugs not only do harm to individuals, but are a scourge to the whole human race. In an age when communications are as well developed and international relations are as close as they are today, no country can effectively control narcotics and addiction, regardless of how effective its control machinery or how excellent its laws may be, without international co-operation. That is because the effect of strict control in one country is usually lost through the laxity of one or more of its neighbours.

According to the statistics and estimates supplied to the eleventh session of the Commission on Narcotic Drugs, there are still several millions of opium smokers, over a million addicts to manufactured narcotic drugs and another several millions of coca-chewers and cannabis users in the world today. These alarming figures indicate that the illicit demand for narcotic drugs is still very great, and it is for all of us to redouble our efforts to wipe out addiction through international co-operation.

Now the United Nations is planning to do away with the series of drug-control conventions dealing with narcotic drugs concluded among nations in the last fifty years or so and replace them with a single, complete convention in order that " the weaknesses and complexities of the current system should be eliminated and new concepts introduced which would bring about both a strengthening and a simplification of the control system ". As was stated during the fourth session of the Commission on Narcotic Drugs, this will have a decisive effect on the future control of drugs in the world. Naturally, in view of the close relationship between China's own effort and the international efforts in the work of opium suppression and as enthusiastic supporters of the cause of narcotic control, the Government and the people of China are most anxious to contribute to this new system the experience they have gained.

Here are several suggestions I wish to make in connexion with the draft Single Convention:

1. That in order to ensure that addiction is an offence against the law and to enable the public to understand its meaning, the draft convention should contain in the first chapter definitions of " drug addiction " and " addict ", as it does regarding illicit traffic.

2. That the title of chapter X should be changed to read " Countermeasures for Addiction ", which should include two additional articles on (*a*) penalties for addicts and (*b*) publicity and education against addiction. (See article VII of the 1925 Geneva Agreement.)

3. That for the sake of humanity the contracting parties should admonish and punish alien residents who are addicts just as they would their own nationals. (See article IX of the 1925 Geneva Agreement.)

4. That if owing to special circumstances a contracting party finds itself unable to enforce the article on " penalties for addicts ", it may take a reservation for a specified period of time which should under no circumstances be unduly long. At the expiration of the period, this article should be made operative.

Treatment of the drug addict at the Lexington (Ky.) hospital

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The present paper is a summary of an article published in Federal Probation, *December 1956. The editors of the* Bulletin on Narcotics *wish to thank the author and* Federal Probation *for their kind permission to publish it.*

This article discusses the treatment of addicts at the United States Public Health Service Hospital at Lexington, Ky., and the characteristics of the addicts as they are seen at that hospital. These addicts are not necessarily representative of addicts in the United States of America. No attempt is made to explain some of the observations made.

The word " addict ", as used in the paper, means a person who is physically and psychologically addicted to an opiate drug or a synthetic drug with opiate-like properties, and who is or has been a patient at the hospital.

I. Introduction

The treatment of a hospitalized drug addict is twofold: treatment of the physical addiction resulting from the pharmacological properties of the drug taken, which is relatively simple, and treatment of the psychological addiction and of the basic mental disorder underlying it, which is relatively complex. Recovery from physical addiction can be attained in a few months, whereas the treatment of the psychological addiction and the social and vocational rehabilitation of the patient is a long and difficult process, especially because it requires the active participation of the patient himself. Hospitalization is important from the point of view of the patient because it removes him from the environment that nurtured his addiction, and from the point of view of society because it prevents the spread of addiction by isolating a principal agent of dissemination — namely, the addict.

In the case of the patient who began his addiction in the course of treatment of an illness by a physician, hospitalization provides an opportunity to terminate the addiction in those whose initiating illness is no longer present. If it is still present, hospitalization and treatment can result in a reduction in the dosage of narcotic drugs or, in most instances, in the elimination of the use of narcotic drugs because of improvement resulting from specific treatment of the disease.

II. The United States Public Health Service Hospital at Lexington

The hospital, created especially to treat drug addicts, was opened in 1935 and is located about five miles from Lexington, Ky. The 1,300 beds are mostly in dormitories, 350 being in the infirmary wards (medical, surgical, psychiatric, tuberculosis and withdrawal). It is a " minimum custody hospital ", and no more than about four prisoners depart without authorization each year.

The hospital is authorized by law to treat federal prisoners and probationers, addicts committed from the District of Columbia, and voluntary patients who are addicted to narcotic drugs as defined in the Federal Law of the United States of America.

The *prisoner addicts* are sent to the hospital by the Bureau of Prisons after conviction in a federal court. The *probationers* are required to remain in the hospital after treatment is completed, and are under supervision on return to their home community. *Voluntary* patients are admitted at their own request if beds are available. The record of their admission, treatment and discharge is treated as confidential.

The hospital accepts females from the whole of the United States, and males from east of the Mississippi (male patients from west of the river are usually treated at the United States Public Health Service Hospital in Fort Worth, Texas). Men and women have quarters in separate parts of the hospital; there is no separation by race or age.

A. *Characteristics of the Addict as an Individual*

Physical addiction to opiate drugs is characterized by two phenomena: *physical dependence*, with its sequel of abstinence syndromes when the opiate is discontinued, and *tolerance*. The addict gets used to some of the effects of the drugs (the analgesic, euphoric and sedative effects which are all-important to him), and because of this tolerance, requires increasing amounts of the drug to obtain the desired effect. Physical dependence and tolerance appear to be related to changes in the sympathetic and central nervous systems [1] and in the endocrine glands.[2]

The *etiology* of drug addiction cannot be given in general terms, because the answers vary with each individual. For some persons the narcotics provide an escape from anxiety, frustration, etc.; for others, narcotic usage is a purely hedonistic experience. For others they provide total satisfaction,

[1] A. Wikler, " Recent Progress in Research on the Neurophysiological Basis of Morphine Addiction ", *American Journal of Psychiatry*, 105 : 329, 1948.

[2] A. J. Eisenman, H. Isbell, H. F. Fraser, & J. Sloan, " 17-Ketosteroid Excretion in a Cycle of Morphine Addiction and Withdrawal, " *Federation Procedings*, 12 : 200, 1953.

so that the addicts have little interest in anything else. The motivation for drug usage has to be replaced by a desire to live without narcotic drugs if treatment is to be successful.

Psychological addiction is related to a basic mental disorder of the patient. Usual diagnostic studies give enough information to establish the presence of a mental disorder. Kolb [3] and later Felix [4] developed classification systems of these disorders that were operationally useful, but these have been superseded by utilization of the nomenclature in the *Diagnostic and Statistical Manual of Mental Disorders* of the American Psychiatric Association published in 1952. The mental disorders most frequently present are personality trait disturbances, sociopathic personality disturbances, psychoneurotic disorders, and personality pattern disturbances. Occasionally patients are admitted with schizophrenic or affective reactions.

The personal history of many patients shows the absence of the father, or a weak father or mother during the patient's childhood. The failure of emotional maturation may be related to these absences or of any constant person with whom identification could occur.

B. *Characteristics of the Addict Population*

The *average daily population* in the hospital has varied relatively little over the years, but changes have occured in its composition — mainly in the great increase in voluntary patients.

The *annual admission rate* has varied considerably, due mainly to fluctuations in the annual rates of voluntary patients.

The *age and race* distribution shows very interesting variations if we compare the situation in 1936 with that in 1956. The typical addict described in Pescor's study of 1,000 admissions [5] in 1936 was: " White male prisoner, 38 years of age, given a two-year sentence for illegal sale of narcotics." The typical addict of 1956 is a Negro male voluntary patient in his twenties.

Whereas the earlier addict preferred morphine, the later prefers heroin. Inasmuch as the first was " subject to some chronic disease, such as heart trouble, arthritis, etc.", the second is free of such afflictions. Whereas the 1936 series in Pescor's study showed 8.9% Negroes, the percentage in 1955 was 52. The age distribution of the white males in 1936 and 1955 was similar (a fairly equal distribution by decades from 20 to 60). In the 1955 study, 70% of the Negro males were under age 30, as compared with 27% of the white males.

The following table gives information about the age of onset of addiction:

	1936	*1955-56*
19 and under	16.5	45.0
20–29	53.2	44.6
30–39	21.1	7.6
40 and over	8.9	2.6
Not given	0.3	—

III. Treatment programme

The treatment programme is based on more than twenty years of clinical experience and research. The planning takes into consideration the individual and group characteristics of the patients, and at the same time the limitations imposed by such circumstances as the number of staff available, the requirements of the law, etc. The goal of the programme — and it is as simple as it is difficult to attain — is to prepare the addicts to return to their home communities and live without using narcotic drugs.

When the addict enters the hospital his treatment programme begins: he surrenders any narcotic drugs he possesses and is immediately subjected to a *physical examination*. If there is a physical dependence, he is admitted to the *withdrawal ward* (if there is no complicating disease requiring admission to some other infirmary ward).

Thus the first stage, if there is a need for it, is the treatment of the *abstinence syndrome*. If a patient has physical dependence on an opiate drug, the severity and time of onset of the abstinence signs will be related to the dosage and the particular drug used. A system of measuring the intensity of the syndrome was developed by Himmelsbach [6] and Kolb.[7] These signs may be precipitated by the use of nalorphine.[8] With competent medical care and use of the methadone substitution method, the discomfort and dangers of the abstinence syndrome are minimal. This method is described in a number of publications by Isbell,[9] Wikler [10] and Fraser,[11] of the Addiction Research Center of the National Institute of Mental Health, which is located at this hospital. The method, in brief, is to administer methadone orally in quantities just sufficient to keep signs of abstinence at a tolerable level and then steadily to reduce the dosage. The treatment of the acute phase of the abstinence syndrome which results from physical dependence on narcotic drugs usually requires less than two weeks. This is followed by a period of convalescence or subacute symptoms lasting about two weeks, when the patient regains his strength, weight, and appetite, but is irritable, restless, and has difficulty in sleeping. Complete recovery from physical addiction takes about four months. The time and severity will vary somewhat according to the degree of tolerance and physical dependence of the

[3] L. Kolb, " Types and Characteristics of Drug Addicts ", *Mental Hygiene* 9 : 300-313, April, 1925.

[4] R. H. Felix, " An Appraisal of the Personality Types of the Addict ", *American Journal of Psychiatry* 1 : 462-467, 1944.

[5] M. J. Pescor, " A Statistical Analysis of the Clinical Records of Hospitalized Drug Addicts ", Supplement No. 143 to the Public Health Reports, 1943.

[6] C. K. Himmelsbach & L. F. Small, " Clinical Studies of Drug Addiction ", Supplement to the *Public Health Reports* : 125, 1, 1937.

[7] L. Kolb & C. K. Himmelsbach, " Clinical Studies of Drug Addiction ", Supplement to the *Public Health Reports*, 128, 1938.

[8] H. Isbell, " Nalline, a Specific Narcotic Antagonist ", *Merck Reports* 62, 2; 23-26, 1953.

[9] H. Isbell, " Medical Aspects of Narcotic Addiction ", *Bulletin of the N. Y. Academy of Medicine*, 31 : 886-901, December 1955.

[10] A. Wikler, " Rationale of the Diagnosis and Treatment of Addictions ", *Connecticut State Medical Journal* 19 : 560-568, (July) 1955.

[11] H. F. Fraser, " Treatment of Drug Addiction ", *American Journal of Medicine*, 14 : 571-577, 1953.

patient, and this in turn is determined by the drug used, duration of use, and daily dosage. When the patient is no longer receiving methadone and the acute abstinence signs and symptoms have abated, transfer from the withdrawal ward to an orientation ward is made. When necessary, patients are transferred to another infirmary ward — medicine, surgery, tuberculosis, or psychiatric.

When the patient leaves the withdrawal ward he is placed under the supervision of an *administrative physician*, who is responsible for co-ordinating and supervising his programme until his discharge from the hospital. These administrative physicians are psychiatric residents, and their work is supervised by staff psychiatrists. The patient may be in individual or group psychotherapy with another psychiatric resident. The administrative physician follows the progress of the patient and, except for prisoners, decides when the patient is ready to return to his home community. This system has been in operation since July 1955 and is based to a large extent on the research of Stanton & Schwartz.[12]

The patient remains in the orientation ward for about two weeks after leaving the withdrawal ward. During this time, group discussions for orientation purposes are held and the patient is interviewed individually by members of the vocational, correctional, social service, and psychiatric staff for diagnostic purposes. The patient's administrative physician prepares a diagnostic summary, which is reviewed by a staff psychiatrist, and the treatment programme for the patient is formulated.

Every patient who is physically able to work *has a job*. Most of the young addicts have had erratic or no work records. One purpose of the work assignment is to enable them to work with other people and to accept authority. Many of them regard authority as hostile and punitive. Constructive relations with authority figures different from the ones they knew permit a modification of previous reaction patterns.

The programme varies from patient to patient. One element, however, is common to all: residence in a drug-free environment for a minimum period of four months. This period initiates the disestablishment of the habit of using narcotic drugs as a pattern of living, to relieve anxiety, or for euphoria. Thus patients who appear to be suitable are offered the opportunity of psychotherapy individually or in groups. In many cases this should be continued after release from the hospital.

Group psychotherapy and activity therapy appear to be more suitable than individual psychotherapy for patients with personality trait or sociopathic disturbances. Because of their emotional immaturity, dependency, and hostility, the most useful programme seems to be one similar to the activity programmes used with disturbed children. The immediate " therapist " is the person with whom the patient spends the most time. In most instances this would be the vocational supervisor. Consideration is given not only to the vocational needs of the patient, but also, when indicated, to the needs of the patient for continued association with a particular kind of staff person. The vocational supervisors are apprised of the patient's problems when this appears to be indicated, and the supervisor can discuss the patient with the administrative physician at any time. Staff psychiatrists provide consultation in discussions with groups of vocational supervisors.

The hospital is not a vocational training school, but it does have a large variety of well-organized and active *vocational training programmes* which it is hoped serve as a medium for nurturing emotional maturation. The educational and vocational training unit chief assists the section chiefs in the design of training programmes preparing patients for " payroll " jobs. The accomplishments of the patients in these programmes are amazing when viewed in the light of their past vocational history or lack thereof. They demonstrate the unactivated potential for change that exists within these patients. Each month the vocational supervisor sends a report to the patient's administrative physician rating the patient on co-operation, attitude, interest, dependability, and progress in skill learning. Ratings have been found to be useful indicators of ability to adapt to living in the hospital. Towards the end of his hospitalization, *assistance in getting employment* is provided.

For many of the patients narcotic drugs were the only source of pleasure in living. One source of pleasure for most people is recreation — reading, athletics, films, television, bowling, music, etc. The hospital attempts to provide the patients with opportunities for developing interests in recreation as one facet of living. These patients are able to participate more readily in passive recreation or individual activities than in any endeavour that requires active co-operation as a team member. Recreation can serve as a vehicle for learning to live with other people and to accept the limitations of behaviour imposed by the rules of the game.

Part of the patient's day and evening is spent in the dormitory with other patients. This presents many opportunities for constructive, destructive, and neutral associations. Since narcotic drugs were the central and sometimes the exclusive preoccupation of the patients before hospitalization, much time is spent in discussions on this subject. Until a few years ago the women patients were in a separate small building a short distance away from the main building. A frequent comment by the staff at that time was that the men spent so much time talking about drugs. Now the comment is that they spend so much time talking about women.

The aid on the dormitory has an important role in the hospital programme. The responsibilities include helping the patients to learn to live with other persons without more than the ordinary amount of strife; helping the patients to learn other adult patterns of living and, most important, the aid can listen to patients' problems and when indicated, provide advice and encouragement. The dormitory aid can get assistance from his supervisor or, if the problem is with regard to a particular patient, then he can consult with the patient's administrative physician. A twelve-month training

[12] A. H. Stanton & M. S. Schwartz, *The Mental Hospital*. New York: Basic Books, Inc., 1954.

programme of classroom, demonstration, and supervised assignments is used to prepare aids for their work.

Social service participates in the diagnostic studies and has the responsibility of identifying the social service needs of the patient. The principal activity is to provide casework services to patients. The problems presented range from personal problems of the patient in the hospital to family problems in a community many miles away. The staff does all the work related to parole and is the liaison with the federal probation officers.

Religion is an important part of the lives of many patients. The hospital has Catholic, Jewish, and Protestant chaplains whose duties include conducting services, individual counselling, and group discussions. The College of the Bible of the Christian Church at Lexington operates a chaplain-training programme at the hospital which is supervised by the Protestant hospital chaplain. The trainees work with patients as a part of their training.

Acting out behaviour of persons with neuroses or character disorders is a problem whether at home, in the community, or in the hospital. For twenty years this hospital had a so-called " adverse behaviour clinic " which has been discontinued. Patients with problems are assisted by the staff members who have direct relations with them. When necessary, the supervisor, the administrative physician, or a staff psychiatrist is available. Action that appears most helpful to the patient is taken.

The *termination of hospitalization* depends on the status of the patient. If he is a prisoner it is determined by the sentence or action of the Board of Parole. If he is on probation it takes place when hospital treatment is completed. If he is a voluntary patient it can be at any time he wishes.

Thus it has been seen that many persons have important roles in the treatment programme at the hospital — the aid on the dormitory, the vocational supervisor, the physician, the social worker, the consultant, etc. It should be realized that completion of hospitalization is *not* completion of rehabilitation for the patient. This can occur only after the patient has left the hospital and returned to his home community.

IV. Results

From the opening of the hospital in 1935 until the end of the fiscal year 1955, 23,625 addicts were admitted a total of 45,058 times.

The results of hospitalization can be expressed by comparing the condition of the patient at the time of discharge with his condition at the time of admission. Patients are classified as " *unimproved* " if physical dependence is present at the time of discharge, or if there is no progress towards freedom from psychological dependence. " *Hospital treatment completed* " means that at the time of discharge there is freedom from physical addiction and enough progress towards freedom from psychological addiction has taken place for discharge to the community to be indicated. " *Improved* " is the status between these two.

In 1955, about one-third of the addict patients admitted stayed in the hospital for such short periods that their condition on discharge was " unimproved " (these were voluntary patients). About one-third of the patients were discharged as " improved ", and one-third reached the status of " hospital treatment completed ".

It would be interesting to know how many patients did not become re-addicted after their hospitalization. Pescor [13] attempted such a study of 4,766 patients discharged from 1936 to 1940. He did determine that 39.9% of the patients had relapsed in periods varying from six months to six years. Twenty-five per cent of those about whom information was available were abstinent. It is interesting to note that prisoners on parole had the best records. This group received the most post-hospital supervision and could not leave the hospital until there was a satisfactory plan for a job, place to live, etc.

From the statistical point of view it is also of interest to study the work done by Rayport [14] on 1,020 male patients, in which he classifies addicts who at first received narcotic drugs from a physician to the point of addiction in the course of treatment for an illness.

V. Conclusions

There are a number of difficulties involved in the treatment of the narcotic addict: for instance, the patient must remain in hospital long enough for the physical addiction to be treated, yet 40% of the voluntary patients leave in less than two weeks. As regards psychological addiction, the patients must have some motivation to live without narcotic drugs, and it is not possible to give such motivation artificially. Even with every care and attention there is no way of knowing whether that motivation does exist or not.

The treatment of physical addiction presents no difficulties if the patient is in a drug-free environment: the methadone substitution method has proved very satisfactory.

(The reports stating that chlorpromazine and reserpine are of value in the treatment of the abstinence syndrome seem to lack a firm foundation.)

It is unfortunate that the treatment of psychological addiction is not as well known and developed as that of physical addiction. The fact is that since it is usually closely related to a mental disorder, only improved methods for dealing with the latter will prove efficacious in the treatment of psychological addiction.

Finally, it should be borne in mind that, if hospital treatment can put a patient on the way to recovery, it cannot provide a life-long immunity and can only *initiate* rehabilitation. This must be completed *after* the patient returns to the community.

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[13] M. J. Pescor, *Follow-up Study of Treated Narcotic Drug Addicts*, Supplement No. 170 to the Public Health Reports, 1943.

[14] M. Rayport, " Experience in the Management of Patients medically addicted to Narcotics ", *Journal of the American Medical Association*, 156 : 684-691, October 16, 1954.

Effect of promedol on the bioelectric activity of the cortex of the brain

(Experimental study)

By V. V. Vasilyeva, K. M. Lakin & P. V. Sergeev
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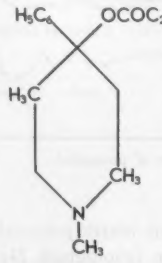
Pain-killers are an important means of pathogenetic therapy in many diseases. The pain impulses accompanying various pathogenetic processes cause excessive irritation to the central nervous system, exhaust the cortex of the brain and help to perpetuate and aggravate the disease. By weakening or eliminating the reception of pain impulses, analgesics prevent over-irritation of the central nervous system and help medically protective inhibitions to develop and the higher regulative mechanisms to resume their functions.

Of the pain-killing substances, promedol — a synthetic substitute for morphine — is of considerable interest. It is a new analgesic, synthetized in 1951 by Academician I. N. Nazarov. In chemical parlance, it consists of hydrochloride of 1,2,5-trimethyl-4-phenyl-4-propionoxypiperidine.



It is a white crystalline powder with a bitter taste. It is soluble in water, alcohol and chloroform, and insoluble in ether and benzol. Promedol solutions have an almost neutral reaction, remain stable when stored and are sterilized by heating to 100° for thirty minutes or to 120° for fifteen minutes. Its pharmacological properties have been studied by M. D. Mashkovsky, V. I. Ishchenko, V. I. Legostev, Siu Bin, L. I. Grebennik, E. N. Guseva and others.

The pain-killing effect of promedol resembles that of morphine and its synthetic substitutes. The organism usually supports it better than morphine or pantopon; it does not cause vomiting or constipation, and has an anti-spasmodic action.

Promedol is used as an analgesic for pains of various origins: ulcer pains, cholecystitis, stenocardia, infarct of the myocardium, colics of the intestines and kidneys, and other diseases accompanied by a pain syndrome.

In surgery, promedol is indicated for various traumata for administering before operations and for post-operative pains. An analgesic effect is also observed in cases of malignant tumours.

In midwifery, promedol is valuable as an analgesic and for hastening the birth. It has no toxic effect on the mother or child (G. A. Tonkikh, A. M. Foy, V. M. Karatygin, Z. I. Roshnova, S. V. Bazanova and others). Despite this relatively wide range of uses, the effect of promedol on the higher nervous activity after one or (and this is particularly important) more doses has not been adequately studied.

In the research test described below, we observed the effect of one or more doses of promedol on the bioelectric activity of the brain cortex in animals.

Method

The experiments were performed on rabbits of both sexes weighing 2,000-3,220 g.

The bioelectric potentials of the animal's brain cortex were recorded by a six-channel electroencephalographic machine. During the test the rabbits were tied down to a special bench and placed in a sound-proof chamber insulated from interference.

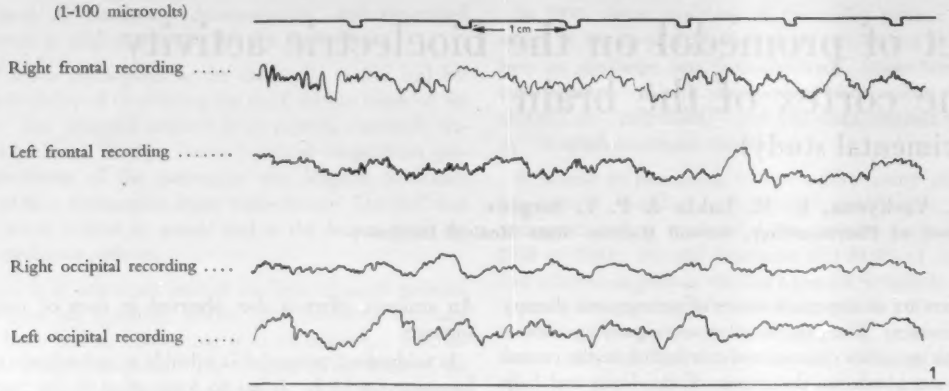
In most cases the electroencephalogram was made with unipolar right and left frontal and occipital localization after the animal had been left for fifteen minutes to adapt itself to the dark inside the chamber. The animal's bio-potentials were first recorded at normal and then at 5, 15 and 30 minutes and 1, 1½, 2 and 3 hours after administration of the promedol in the form of varying doses of a 1% aqueous solution.

Results

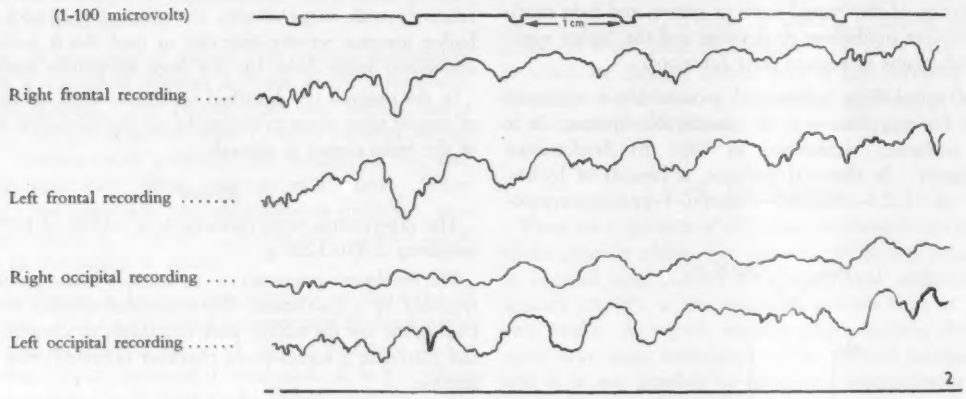
In experiments with a single subcutaneous injection of promedol in doses of 0.25, 0.5 and 1 mg/kg, no marked changes in the brain cortex potentials were observed.

With doses of 3 to 5 mg/kg, marked changes developed. The number of slow waves (1 to 6.5 c/s) and alpha waves (7.5 to 12 c/s) increased and the number of beta waves (15 to 30 c/s) and faster ones (30 c/s and over) decreased. The amplitude of the bio-electrical waves increased. These deviations were particularly marked 30 and 60 minutes after injection but became more moderate after 2½ to 3 hours, when the waves more or less returned to their original pattern.

In the case of rabbit No. 12 before injection, for example, irregular slow waves predominated on the EEG as the background to a large number of fast waves (photograph No. 1). In particular, on a section of the left frontal recording showing the bio-potentials for five seconds there were 10 slow, 14 alpha



Photograph No. 1. — Original condition. Rabbit No. 12, weight 2,400 g



Photograph No. 2. — 30 minutes after a 5 mg/kg subcutaneous injection of promedol

and 80 beta waves, out of a total of 107 waves in all. The average voltage of the bio-potentials, calculated with a planimeter, was 5.13 microvolts.

On the right occipital recording there were 12 slow, 20 alpha and 30 beta waves, while the total number of waves was 72. The average voltage was about 3.4 microvolts.

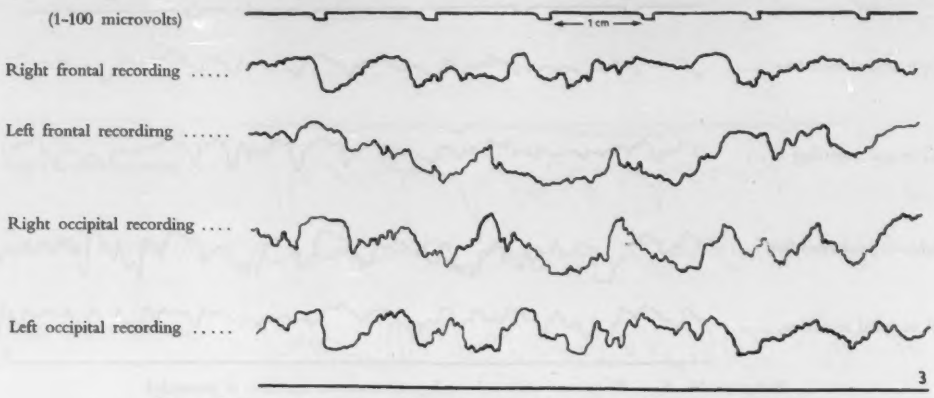
Thirty minutes after a 5 mg/kg subcutaneous injection of promedol. the EEG showed high slow waves as the background to a large number of fast waves of very small amplitude (photograph No. 2). On the left frontal recording the number of alpha waves increased from 14 to 19 and the number of slow waves from 10 to 14. The frequency of the slow waves dropped from 5-6 to 1-3 c/s, the number of beta waves from 80 to 29 and the total number of waves from 107 to 70. The average voltage rose from 5.13 to 11.33 microvolts.

On the right occipital recording the slow waves increased in number from 12 to 19 and were very long. The number of beta waves dropped from 30 to 9 and the total number of waves from 72 to 55. The average voltage rose from 3.4 to 7.2 microvolts.

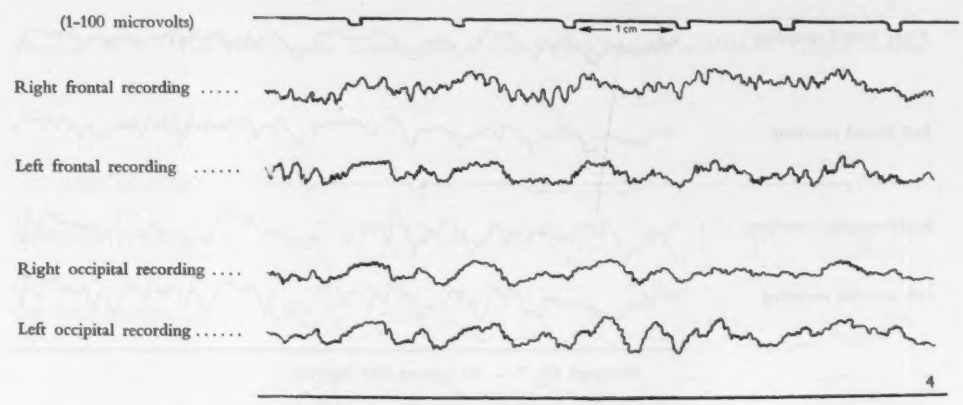
After 3 hours the brain cortex potentials were almost back to their original pattern (photograph No. 4).

Papers by various writers (S. A. Sarkisov, V. S. Rusinov, M. N. Livanov, P. I. Spilberg, P. I. Gulyaev and others) have shown that a decrease in the number of fast waves and an increase in the number of slow waves indicate an increase in the inhibiting processes in the brain cortex. It would appear from the EEG changes shown above that the doses of promedol studied cause the inhibiting processes in the brain cortex to predominate. This tallies with the data obtained by N. D. Mashkovsky, V. I. Ishchenko, V. I. Legostev, O. N. Voevodina, Siu Bin and others, who found, by the conditioned reflex and the impulse aggregation methods, that promedol in these doses reduces the excitability of the cortex of the cerebral hemispheres.

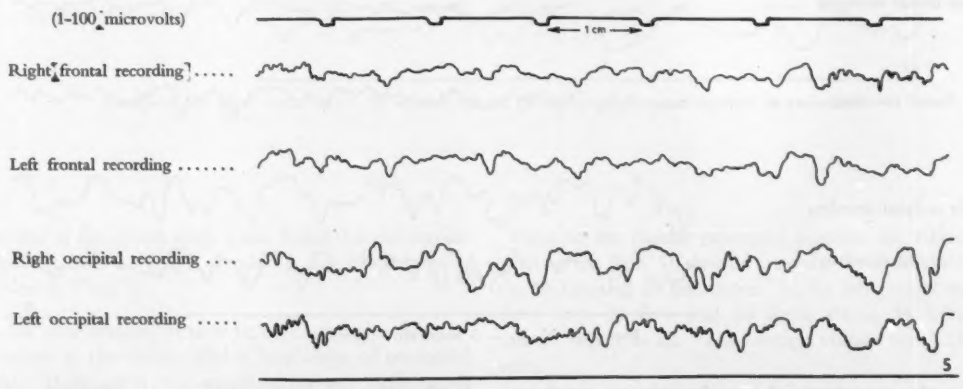
In clinical pratice, a highly important criterion for determining the value of analgesics is habituation and addiction to them by the patient. Much attention has been given to this question in experimental and clinical tests of analgesics (articles by H. Isbell, H. F. Fraser, A. Wikler and others), but an adequate study of habituation to promedol has yet to be made. Whereas B. I. Legostev, Siu Bin and E. N. Gu-



Photograph No. 3. — 60 minutes after a 5 mg/kg subcutaneous injection of promedol



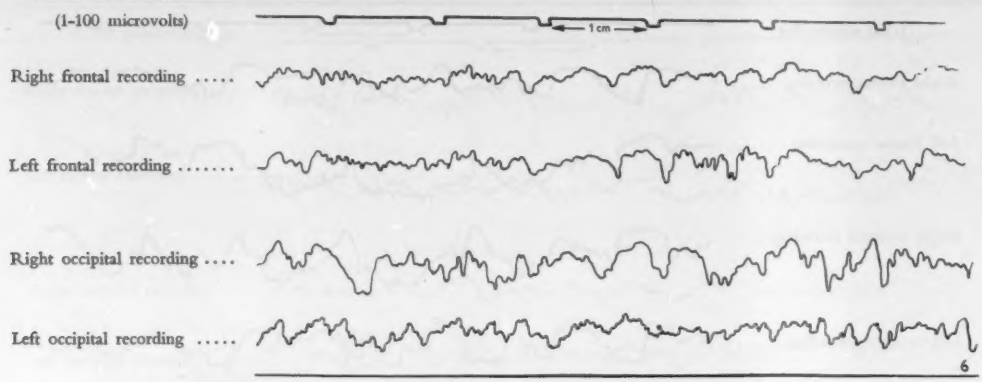
Photograph No. 4. — 3 hours after promedol injection



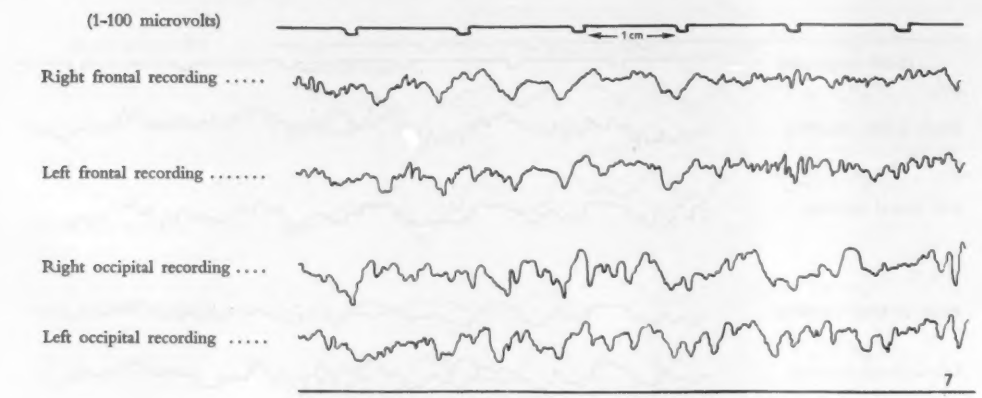
Photograph No. 5. — After two weeks of daily 5 mg/kg promedol injections. Original condition before regular injection

seva say that habituation occurs, M. D. Mashkovsky and V. I. Ishchenko state that none was observed in rats and dogs after testing with repeated promedol injections.

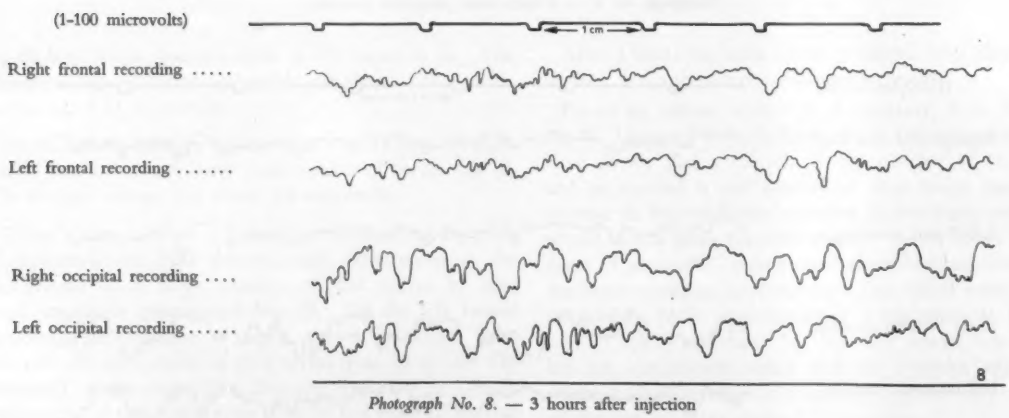
The next stage of our research was to observe the changes in the brain cortex potentials after the rabbits had been given promedol injections over a period of two weeks.



Photograph No. 6. — 30 minutes after a 5 mg/kg subcutaneous injection of promedol



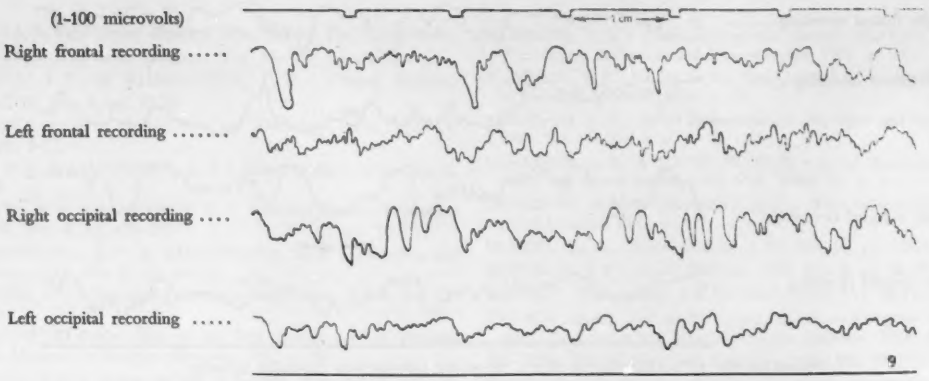
Photograph No. 7. — 60 minutes after injection



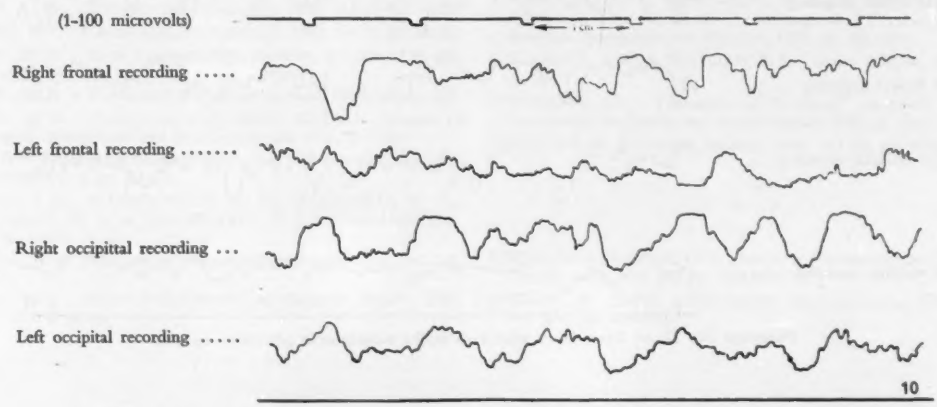
Photograph No. 8. — 3 hours after injection

The animals were given a 3-5 mg/kg subcutaneous injection twice a day. Every three days the changes in the bio-electric potentials due to regular promedol injections were ascertained.

The experiments showed that after promedol had been taken for a week the succeeding injection always produced the changes in the electrical waves described above—i.e., an increase in the number of slow and alpha waves, a larger number of fast waves and an increase in the amplitude of the bio-electrical waves. But these changes lasted a shorter time, and after 1-1½ hours the EEG wave pattern resembled the original one.



Photograph No. 9. — Two weeks from the commencement of daily 5 mg/kg injections of promedol. Original condition



Photograph No. 10. — Same rabbit, 30 minutes after a 15 mg/kg subcutaneous injection of promedol

By the end of the second week it was found that the regular promedol injection no longer produced this effect (photographs Nos. 6, 7 and 8).

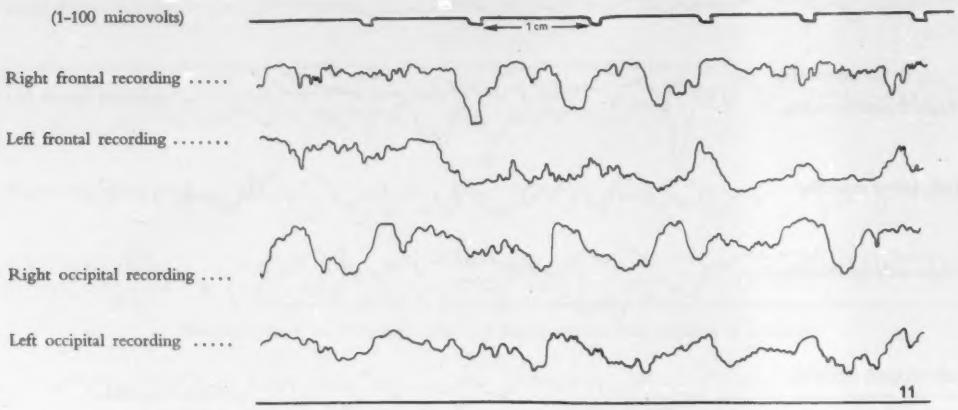
From the data obtained it may be concluded that habituation develops in the rabbits after a long series of promedol injections. Habituation was expressed in our experiments by the reaction of the bio-electrical waves to the regular injection becoming weaker and finally disappearing.

In rabbits which had been injected over a period of two weeks these changes in the bioelectrical waves occurred only when the dose was increased to 10-15 mg/kg.

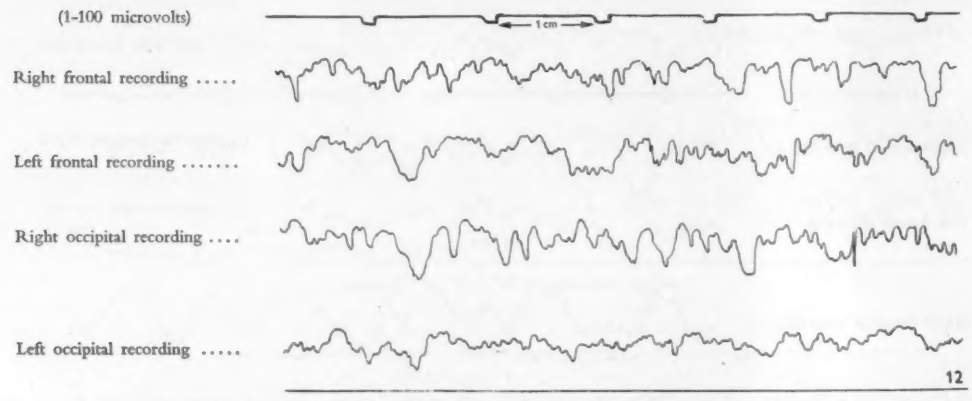
Prior to the regular promedol injection the rabbits' EEG (photograph No. 9) showed irregular slow waves forming the background to fast waves. In the left frontal recording there were 10 slow and 16 alpha waves, 56 beta waves and 97 waves in all. The average voltage was 7.13 microvolts.

In the right occipital recording there were 14 slow, 19 alpha and 34 beta waves, and 71 waves in all. The average voltage was 10.33 microvolts.

After the rabbit had received a 15 mg/kg injection the EEG showed high slow waves (photograph No. 10). The number of fast waves decreased.



Photograph No. 11. — 60 minutes after a 15 mg/kg subcutaneous promedol injection



Photograph No. 12. — Three hours after a 15 mg/kg subcutaneous promedol injection

In the left frontal recording the slow waves increased in number from 10 to 15 and sharply decreased in frequency. The number of beta waves dropped from 56 to 24 and the total number of waves from 97 to 70. The average voltage rose from 7.13 to 9.4 microvolts.

Although in the right occipital recording the slow waves showed practically no change in number (15), their frequency decreased from 5-6 to 1-3 c/s. The number of beta waves dropped from 34 to 21 and the total number of waves from 71 to 60. The average voltage rose from 10.33 to 12.2 microvolts.

In this case, however, the pattern of the bioelectrical potentials approximated to the original one three hours after the promedol injection (photograph No. 12).

Conclusion

It may be conclued from our experiments that in rabbits given subcutaneous injections of 0.25-0.5-1 mg/kg of promedol, no discernible changes in the brain cortex potentials occur.

When the dose was increased to 3-5 mg/kg the number of alpha waves and slow waves increased. Their frequency decreased considerably and their amplitude increased. The number of fast waves invariably fell. This may indicate the predominance of inhibiting processes in the central nervous system.

With repeated injections, the animals develop an habituation to promedol, as was indicated by the disappearance of the normal reaction of the bioelectrical brain-waves to regular injection.

An intensification of the inhibiting process in these animals can be brought about only by increasing the dose to 10-15 mg/kg. This is evidence of a decrease in the sensitivity of the central nervous system to promedol and the occurrence of habituation to it.

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Accumulation and distribution of the main alkaloids in the opium poppy in the course of its ontogenesis

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(All-Union Scientific Research Institute for the Study of Medical and Aromatic Plants)

The laborious nature of the processes whereby opium is obtained, together with the great value of the alkaloids obtained from it, has led research workers to look for other kinds of raw material from which to obtain substances of this group. Research has shown (1-11) that alkaloids occur not only in the opium, but also in the poppy plant. After the discovery of methods of obtaining alkaloids from poppy straw (12-14), various countries began to extract alkaloids (in most cases morphine only) from the capsules and stems of the oil-bearing poppy, which are waste products of poppy-growing for oil production. The possibility of using the stems (straw) to obtain codeine, narcotine, papaverine, thebaine and narceine, which are extracted exclusively from opium, was still a moot point until recently, for there were only scrappy and often contradictory data on whether the stems contained them. The possibility of using for those purposes varieties of poppies cultivated for the production of opium also remained unexplored, for this would make it impossible to obtain opium as the main product and could be justified only where it was, unquestionably, economically advantageous.

These points could be settled only by thoroughly studying the laws governing the accumulation and distribution of alkaloids in the various parts of the opium poppy, with a view to determining the possible types of raw material and the proper times for harvesting it.

Accordingly, in 1948-49 we made a study of the dynamics of the accumulation of morphine, codeine, thebaine, narcotine, papaverine and narceine, as well as of total alkaloids in the whole plant and individual organs throughout the growing period. The subject of research was a variety of opium poppy grown near Przhevalsk in Kirghizia, at 1,800 metres above sea-level. The investigation covered the young shoot, rosette, stalk formation, bud formation, flowering and technical (opium) and biological (seed) maturity stages, and dealt with the leaves (upper, middle and lower), stalk, root and reproductive organs, the specimens being analysed after hot-air conservation (105°C for 20 minutes) and air drying. Total alkaloids were isolated by the widely used alcohol-dichlorethane method (10) and individual alkaloids separated and identified by B. A. Klyachkina's method (15), from 20 to 400 plants being used in each case.

The study of the dynamics of accumulation of the dry substance showed that it accumulates steadily until biological maturity, and continues to do so at different rates according to the stage of development, maximum accumulation occurring during the period in which the reproductive organs appear and develop (bud formation, flowering and technical maturity). At the end of the growing period the substance is mainly concentrated in the capsules (up to 39% of the total weight of the plant) (see table 1).

The study of the dynamics of the accumulation of total alkaloids revealed that this too proceeds as the plant develops, right up to biological maturity, and is most rapid during the period between flowering and technical maturity. Accumulation at this stage is so vigorous that within a period of fifteen to eighteen days, the plant accumulates over 50% of the total quantity of alkaloids formed during the entire growing period (about 130 days). Up to 48% of this is concentrated in the capsules (see table 2).

The accumulation of alkaloids in the opium poppy is closely connected with the growth of its reproductive organs, which are the main alkaloid repository and are responsible for the intensive formation of alkaloids and their movement from other organs during that period.

Comparing the figures for increase of dry substance per unit of time with those for the alkaloid accumulation rate, we find that the two quantities are correlated: the more dry substance the plant accumulates per unit of time, the greater its capacity for accumulating alkaloids. This phenomenon, which was observed over a period of two years, confirms earlier observations (16, 17) that the formation of opium alkaloids occurs in young and vigorously developing cells. It follows that the more intensive the accumulation of dry substance in g per unit of time, the more rapidly the alkaloid content of the plant must also be acccumulating. Tests have shown that this correlation not only occurs in the whole plant, but can also be traced in the reproductive organs. On testing the alkaloid content of the capsules of various varieties of opium poppy it was found that a high alkaloid content always corresponds with a rapid rate of growth of dry substance during the period from flowering to technical maturity. This correlation could presumably be put to practical use in selecting varieties of poppy with a high alkaloid content.

The accumulation of the various main alkaloids in the plant is somewhat different from that of total alkaloids taken together (see table 3). Accumulation already begins at the time the shoots appear, when all the alkaloids can be identified in the plant, but proceeds very slowly until the stage of stalk formation. During this period, morphine and narcotine predominate, followed by papaverine, codeine, thebaine and narceine. Thereafter the accumulation of morphine and narcotine proceeds almost at the same pace

TABLE 1

Accumulation of dry substance by the plant by stage of growth

(g of absolute dry weight per plant — 1950 experiment)

Organ	Stage of development						
	Young shoots 15 May	Rosette 2 June	Stalk formation 27 June	Bud formation 6 July	Flowering 11 July	Technical maturity 28 July	Biological maturity 11 August
Reproductive organs	—	—	—	3.05	5.14	33.99	55.45
Leaves	—	1.06	16.95	28.18	32.64	39.54	30.22
Upper	—	—	3.05	10.00	12.14	19.84	16.56
Middle	—	—	9.13	11.27	13.60	12.79	10.60
Lower	—	—	4.77	6.91	6.90	6.91	3.06
Stalk	—	—	4.68	20.32	27.43	41.85	40.60
Root	—	0.08	2.49	6.68	9.51	11.64	13.96
Whole plant	0.017	1.14	24.12	58.23	74.72	127.02	140.23
Increase in dry substance, in g per day		0.06	0.92	3.79	3.30	3.76	0.73

until the stage of technical maturity, after which the amount of morphine decreases while that of narcotine goes on increasing until the plant dies off. The accumulation of codeine, third in point of quantity, proceeds simultaneously with that of morphine, but goes on after technical maturity until biological maturity. The accumulation of thebaine, like that of morphine, ceases at technical maturity.

Comparing the accumulation of morphine and codeine, and especially their rate of accumulation in mg per day per unit of dry substance in the plants, we find that the plant cells are better able to accumulate morphine when they are young, and better able to accumulate codeine when they are older. For example, an increase in the morphine accumulation rate occurs when the plant is growing rapidly and forming new tissues (the stalk formation stage) whereas the codeine accumulation rate increases during the periods of slow growth of the already developed tissues (the rosette and flowering stages). Since morphine and codeine are the most closely related of the opium alkaloids in structure, it may be assumed that conversion of morphine into codeine occurs as the plant grows older, owing to the higher methylation capacity of old tissues (18). Since thebaine accumulation decreases after technical maturity while accumulation of codeine continues up to biological maturity, it may be assumed that the plant's capacity to form alkaloids of the phenanthrene series as the tissue's age changes, is as follows: morphine — thebaine — codeine.

The course of accumulation of papaverine and narceine resembles that of narcotine and continues up to biological maturity, when it reaches its peak. Examination of the rate of accumulation of narcotine and papaverine shows in a number of cases that narcotine accumulation is more rapid where papaverine accumulation ceases or slows down and *vice versa*, which indicates that a correlation exists between the formation of these two alkaloids. Since narcotine appears in the plant before papaverine and its accumulation rate increases in periods when new tissues are being formed, which is not the case with papaverine, it may be assumed that as the plant ages its tendency to form and accumulate these alkaloids shifts from narcotine to papaverine. In the case of narceine no pronounced correlation with the processes of the plant's growth and development is observed. Judging from the course of its accumulation in individual organs and the daily fluctuations of narcotine and papaverine, it may be assumed that narceine represents a proto-alkaloid or intermediate substance in the formation of these two alkaloids.

In the light of the foregoing, it is interesting to follow the amount of the main alkaloids contained by the plants in relation to factors accelerating or retarding their growth,

TABLE 2

Accumulation of total alkaloids in the plant by stage of development

(mg per plant)

Organ	Stage of development						
	Young shoots	Rosette	Stalk formation	Bud formation	Flowering	Technical maturity	Biological maturity
Reproductive organs	—	—	—	23.00	42.83	487.71	624.97
Leaves	—	3.85	41.45	114.12	132.72	268.84	180.46
Upper	—	—	11.12	55.99	62.89	145.80	93.23
Middle	—	—	25.56	38.30	47.61	82.39	69.00
Lower	—	—	4.77	19.83	22.22	40.65	18.23
Stalk	—	—	12.15	40.02	86.42	137.69	227.36
Root	—	0.53	11.72	35.08	66.56	102.64	62.54
Whole plant	0.002	4.38	65.32	212.30	328.50	996.90	1,095.30

TABLE 3

Accumulation of the main alkaloids in the opium poppy in the course of its ontogenesis

(mg per plant — 1950 experiment)

Alkaloids	Stage of development					
	Rosette	Stalk formation	Bud formation	Flowering	Technical maturity	Biological maturity
Morphine	0.703	26.93	49.70	58.63	228.17	193.85
Codeine	0.275	4.29	34.63	25.88	62.29	89.57
Thebaine	0.014	2.45	6.59	2.52	23.43	9.50
Narcotine	0.355	24.70	23.02	50.26	144.16	208.43
Papaverine	0.323	1.45	5.09	5.66	16.97	25.77
Narceine	0.080	3.81	5.00	4.71	15.23	43.55
Others	2.920	1.18	79.55	177.75	570.54	545.00

since the likelihood is that accelerating factors promote accumulation of codeine and papaverine and retarding factors that of morphine and narcotine. Checking the alkaloid accumulation rate in the 1949 and 1950 experiments against meteorological data, it was found that for morphine and narcotine accumulation the essential condition is sufficient humidity and a relatively low optimum temperature; for papaverine, higher temperatures and low humidity; and for codeine and papaverine, low temperatures and high humidity. A study of the effect of climatic conditions on the amount of individual alkaloids contained in opium (19) revealed a similar picture.

In the course of our investigation, we discovered, for the first time, a big difference between total alkaloids and the total amount of the six main ones. In the period from flowering to biological maturity this difference is equal to the sum of all the main alkaloids. This fact has not so far attracted the attention of research workers, and no practical advantage has been taken of it in connexion with the use of opium-bearing types of poppy for extraction purposes, although the discrepancy may result in a number of difficulties in processing. For example, since substances involved are in the nature of bases, they may complicate the process of separating and purifying alkaloids and decrease the efficiency of absorbents, etc. As we have shown, the most rapid accumulation of the main alkaloids in the poppy plant occurs during the period from flowering to so-called technical maturity, which is also the period chiefly responsible for the accumulation of the above-mentioned bases. Since, in addition, the ratios of the alkaloids to one another fluctuate greatly during this period, the assumption is that the composition of the opium will also fluctuate greatly according to the dates at which the capsules are cut and the opium is obtained. Another thing which is highly specific to the poppy is a sharp reduction in the rate of accumulation of alkaloids (codeine excepted) during the flowering period.

The course of accumulation of the main alkaloids in individual organs is to some extent specific to each organ, obviously depending on the physiological part it plays. In the leaves of the opium poppy, alkaloid accumulation begins at the time of their formation and continues until technical maturity in the case of morphine, thebaine and narcotine and until biological maturity in that of codeine, papaverine and narceine (see table 4). But the relative contribution of the leaves to the plant's total alkaloid content steadily declines as the plant develops. For example, whereas the leaves contain up to 68% of the total amount of morphine and up to 74% of that of narcotine during the stalk formation stage, the figures are only 30% and 26% during the technical maturity stage and even less, 12% and 9%, at the biological maturity stage. Since the accumulation of alkaloids in the plant as a whole goes on until biological maturity, the decrease in the alkaloid content of the leaves after technical maturity can hardly be ascribed to the destruction of the alkaloids. It is more likely that there is a migration of alkaloids into other organs, particularly into the capsule.

In general, the accumulation of alkaloids in the stalk and root resembles that in the leaves (see tables 5 and 6), except in the cases of narcotine and papaverine. These two organs, however, make only a very small contribution to the plant's

TABLE 4

Accumulation of alkaloids in the leaves of the poppy in the course of its ontogenesis

(mg per plant — 1950 experiment)

Alkaloids	Development Stage					
	Rosette	Stalk Formation	Bud formation	Flowering	Technical maturity	Biological maturity
Morphine	0.58	18.20	28.16	27.95	69.15	23.50
Codeine	0.24	1.93	11.22	10.00	9.57	11.86
Thebaine	0.11	0.77	1.96	1.21	5.19	3.22
Narcotine	0.10	18.40	14.90	27.63	37.88	19.57
Papaverine	0.03	0.75	3.21	3.64	1.92	2.78
Narceine	0.07	2.85	2.71	1.65	2.42	9.11

TABLE 5

Accumulation of the main alkaloids in the stalk and root of the poppy in the course of its ontogenesis

(mg per plant — 1950 experiment)

Alkaloid	Stage of development					
	Rosette	Stalk Formation	Bud formation	Flowering	Technical maturity	Biological maturity
			In the stalk			
Morphine	—	3.95	10.38	11.79	25.95	22.33
Codeine	—	1.96	15.64	7.41	11.30	19.49
Thebaine	—	0.93	2.84	0.27	4.18	0.40
Narcotine	—	1.78	3.25	7.27	24.78	16.16
Papaverine	—	0.20	1.17	1.01	2.51	1.14
Narceine	—	0.68	1.69	1.81	3.31	21.92
TOTAL ...	—	12.15	40.02	86.42	137.69	227.36
			In the root			
Morphine	0.12	4.38	4.81	8.87	13.38	8.00
Codeine	0.03	0.40	4.25	1.26	2.73	4.47
Thebaine	0.003	0.75	0.87	traces	0.81	0.15
Narcotine	0.26	4.53	2.57	4.79	5.21	6.84
Papaverine	0.005	0.49	0.29	1.33	1.16	0.50
Narceine	0.01	0.28	0.33	0.45	0.51	1.98
TOTAL ...	0.53	11.71	35.08	66.56	102.64	62.54

alkaloid content. The root, which is small during the technical maturity period, accounts for less than 7% of the total amount of alkaloids in the plant and is of no possible practical value. The stalk contains 11% to 17% of the alkaloids during this period, but since it is large in bulk (32% to 34% of the whole plant), its alkaloid content is so low percentagewise (morphine 0.06%, papaverine 0.006% etc.) that no method of obtaining alkaloids from it is likely to be devised in the near future.

TABLE 6

Accumulation of the main alkaloids in the poppy's reproductive organs

(Percentage of absolutely dry substance (numerator) and mg per plant (denominator) — 1950 experiment)

Alkaloid	Development stage			
	Bud formation	Flowering	Technical maturity	Biological maturity
Morphine	0.208 / 6.35	0.311 / 16.00	0.452 / 119.69	0.505 / 140.02
Codeine	0.115 / 3.51	0.14 / 7.20	0.146 / 38.68	0.194 / 53.79
Thebaine	0.03 / 0.92	0.02 / 1.03	0.05 / 13.25	0.019 / 5.27
Narcotine	0.075 / 2.29	0.205 / 10.57	0.288 / 76.30	0.598 / 165.86
Papaverine	0.014 / 0.43	0.017 / 0.87	0.041 / 10.86	0.077 / 21.35
Narceine	0.009 / 0.27	0.015 / 0.78	0.034 / 9.11	0.038 / 10.54
TOTAL, in mg	23.10	42.83	487.71	624.96

The most rapid accumulation of alkaloids occurs in the reproductive organs (see table 6), where accumulation continues, in the case of all the alkaloids except thebaine, up to biological maturity.

The individual alkaloids accumulate in the capsules at markedly different rates: narcotine outstrips morphine and becomes the main alkaloid in the capsules by the time the seeds are fully ripe.

The capsule of the opium poppy is the main organ and the richest one in alkaloids, and at the end of the growing period contains up to 70% of all the morphine in the plant, up to 80% of the narcotine and papaverine and up to 60% of the codeine and thebaine, and this makes it a suitable raw material source for obtaining those alkaloids. The best time to pick the opium poppy for extraction purposes is the stage of biological maturity if the capsules are used, and the stage of technical maturity if the plant is harvested whole. As the use of the whole plant presents a number of difficulties (drying the fresh stem, large number of ballast substances, loss of seeds and low alkaloid content), the best raw material is the capsule.

Conclusions

1. The rate of accumulation of alkaloids in the opium poppy depends upon the rate of accumulation of dry substance in the plant. Where this is high (in terms of g of dry substance per day) the plant has a higher alkaloid content.

2. The accumulation of alkaloids in the plant occurs from the time of the appearance of the shoots up to biological maturity and is most rapid in the period from flowering to technical maturity.

3. Accumulation of the main alkaloids depends on the age of the plant. Morphine and narcotine accumulate most rapidly when it is young; codeine and papaverine as it ages.

4. Apart from the main alkaloids, considerable quantities of basic substances, the nature of which still remains to be ascertained, occur in the opium poppy.

5. The amount of alkaloids in individual organs depends on the stage reached in the plant's development. The organ with the highest alkaloid content is the capsule at the stage of technical and particularly of biological maturity, when it contains an average of about 70% of all the main alkaloids in the plant.

6. Opium poppy capsules harvested at the stage of biological maturity, and the whole plant harvested at the stage of technical maturity, may be used as raw materials for extraction.

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The analysis of barbiturates by the pressed bromide sampling method and infra-red spectrophotometry

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The barbiturates present a formidable group of compounds to analyse from small samples and to identify specifically from one another. The infra-red absorption spectra are their most fundamental characteristic physical property in the solid state. Recordings of the individual infra-red absorption spectra of the barbiturates provide the basis of an excellent reference file. If this reference file is established on a quantitative basis, then critical procedures for qualitative and quantitative analyses of these closely related compounds can be developed.

The history, chemical structure and synthesis of the barbituric acids have recently been described by Levi (1) in the *Bulletin on Narcotics.*

Instrumental procedures, including ultra-violet and infra-red absorption analytical methods have been developed for the analysis of barbiturates (2), along with procedures including colour reactions, titrimetric procedures, microcrystal tests, paper chromatography and complex derivatives (3, 4).

Experimental

The spectra were recorded on a Perkin-Elmer model 21, double-beam, optical null infra-red spectrophotometer. The samples contain 0.002 g of barbiturate thoroughly powdered and mixed with 0.998 g of spectral pure potassium bromide. From the 1.000-g mixtures 0.300 g were weighed and then pressed into 13-mm discs, approximately 1 mm thick, in a KBr die under 20,000 lb./sq.in. pressure. These discs were mounted directly in the light path of the infra-red spectrophotometer by means of a micro-sample adapter. Sampling equipment and techniques are described in detail in the references (5, 6) cited in the bibliography.

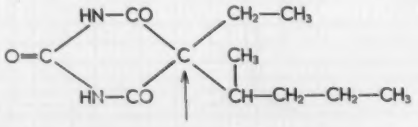
Identification of a Barbiturate by its Characteristic Infra-red Spectrum

The general empirical method of identifying an unknown substance by directly comparing its characteristic infra-red spectrum with the infra-red spectra of known compounds was described by the author in a previous contribution on narcotics to the *Bulletin on Narcotics* (7). In the present article, a short summary is presented of the method by which an individual barbiturate may be identified by a detailed consideration of the individual group frequencies. The infra-red spectrum is a unique and characteristic physical property of that substance based upon the fundamental functional groupings in the molecule. A study of the prominent features of the spectrum will often yield sufficient structural information to identify the nature of the unknown barbiturate.

The infra-red spectra of fourteen of the most important barbiturates were recorded as described above and illustrated in figures 1 to 14. A graphic summary of the prominent features of these spectra is shown in figure 15. The intensity of absorbence is represented by the height of the lines at the respective frequency or wavelength.

An examination of the resultant diagram shows all the compounds to have a band about 2.90 and a strong band at 3.10 to 3.15. According to Bellamy (8), infra-red spectra of complex molecules, such as cyclic lactams in the solid state (KBr pressed bromide samples fit this description) show strongly a band at about 3.15 (NH hydrogen bonded) and more weakly free NH at 2.92. These cyclic lactams bear a strong resemblance to the barbiturates, the grouping (CO-NH-CO) is associated with a single NH frequency at about 3.13. Secondary amides show a band at about 2.9, displaced to about 3.1 in the solid state. There seems scarcely any doubt that the 3.1 band in these compounds is hydrogen bonded NH.

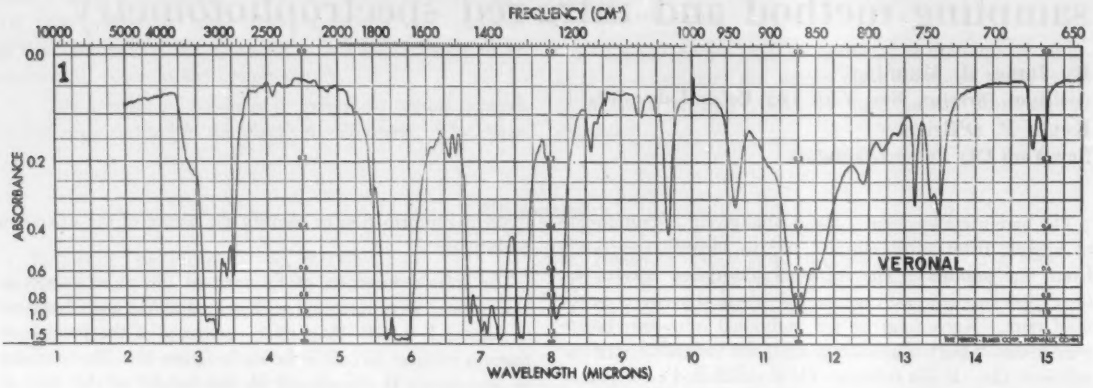
Some, but not all of these compounds show a strong band or bands at about 6.4. The " amide II " bands in secondary amides (which may be NH bending frequencies) occur from about 6.37 to 6.60 in solids. In nearly all these compounds, there is a feeble band at about 6.5 — 6.6, if the strong bands at about 6.4 are absent. Possibly the whole group are " amide II " bands, although there is no apparent explanation of why they should be so much stronger in some compounds than in others. The strong bands at about 6.4 are present when the di-alkyl substituted C-atom carries propyl or butyl groupings such as in

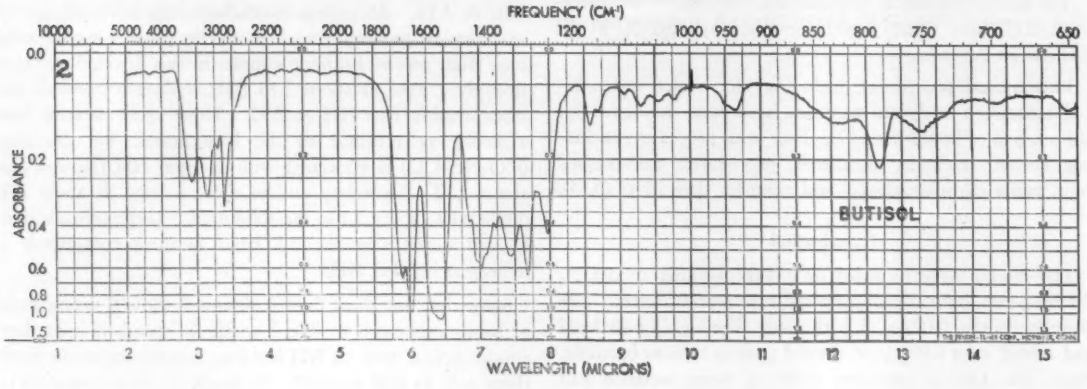


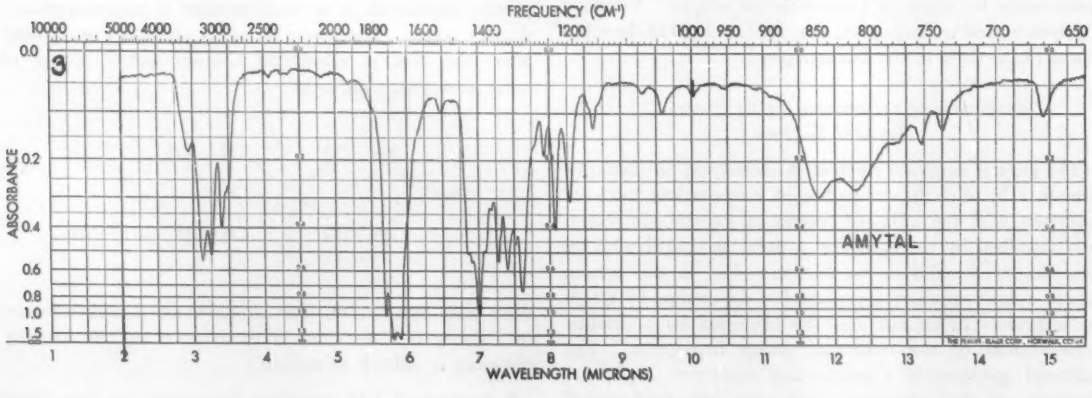
Why their presence on this carbon atom should influence the " amide II " vibrations, if the latter is an NH bending vibration, is difficult to explain.

A mixture of CH stretching frequencies, as they occur in CH_2 and CH_3 groups of relative intensities, governed by the number of CH_2 and CH_3 groups is to be expected in these

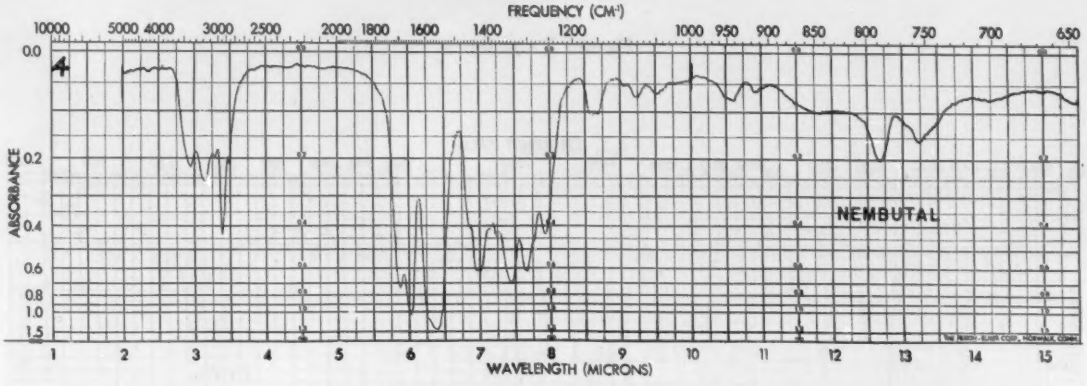
Figures 1 to 3

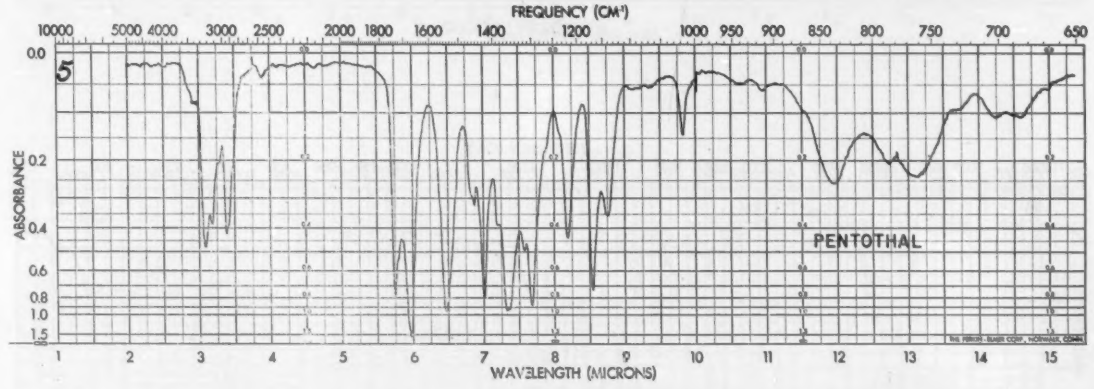


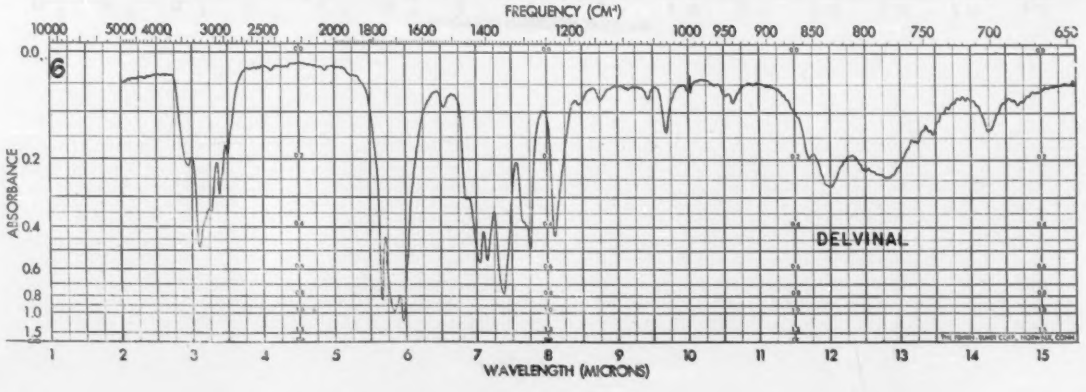




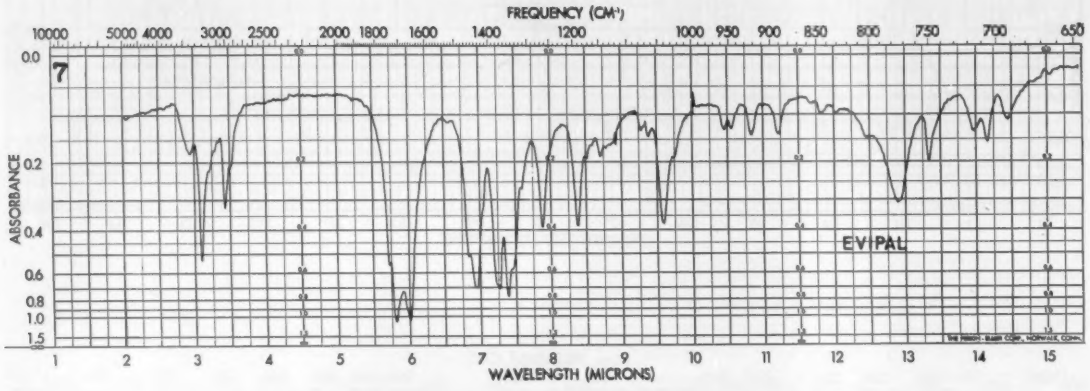
Figures 4 to 6

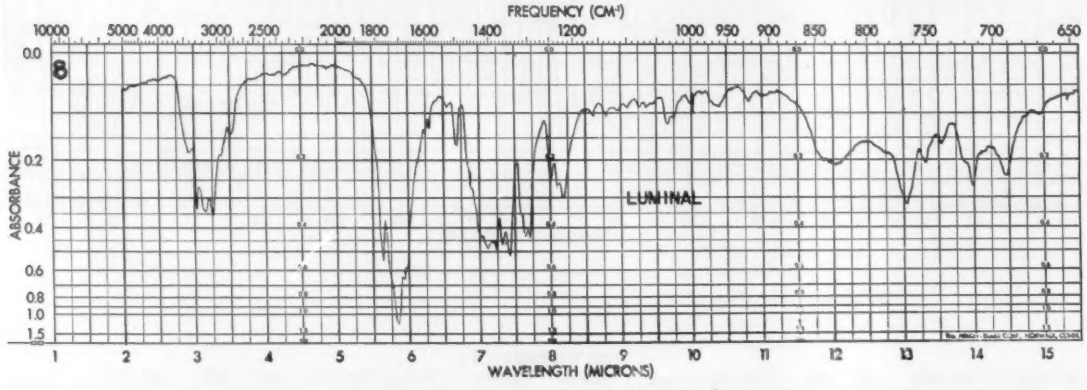




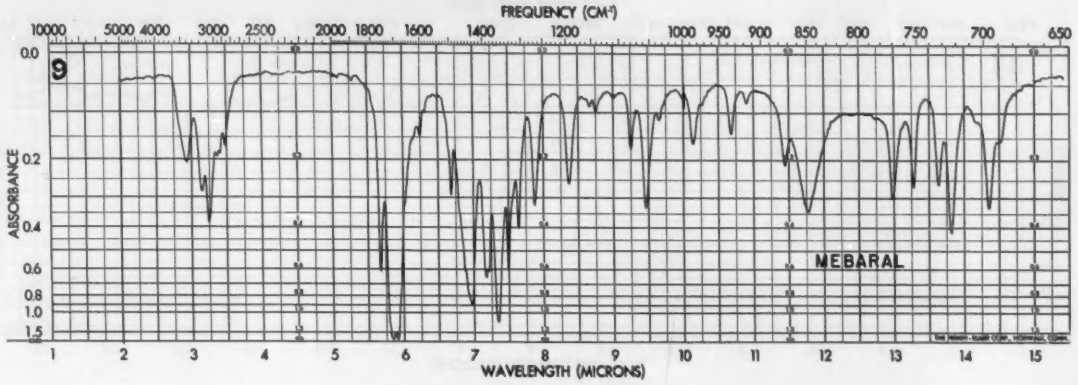


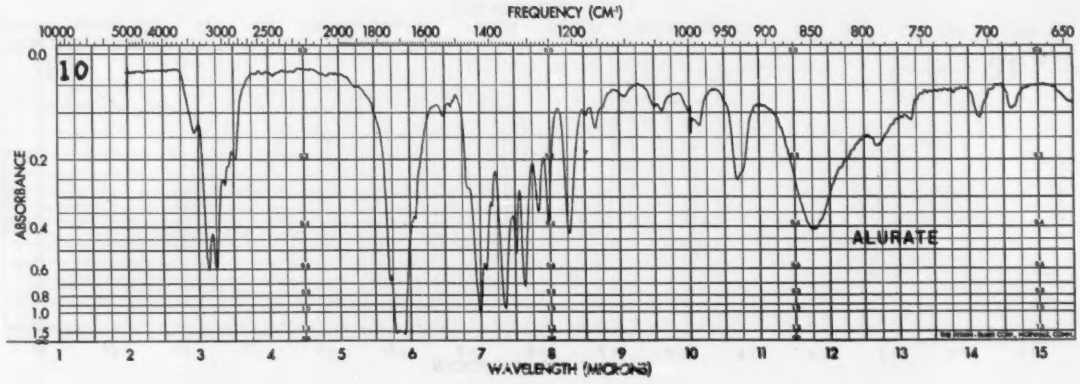
Figures 7 and 8



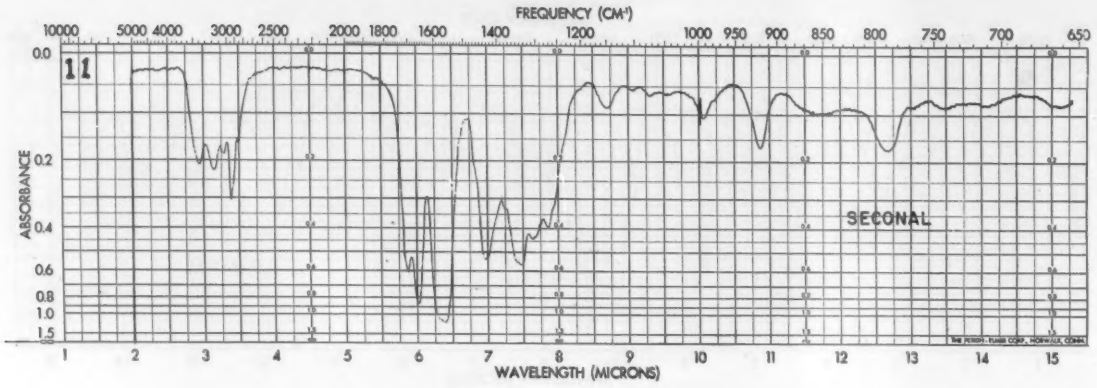


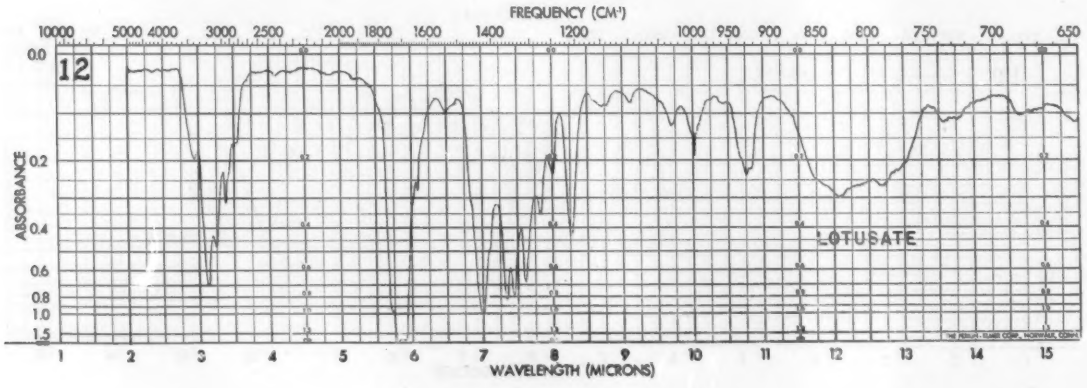
Figures 9 and 10



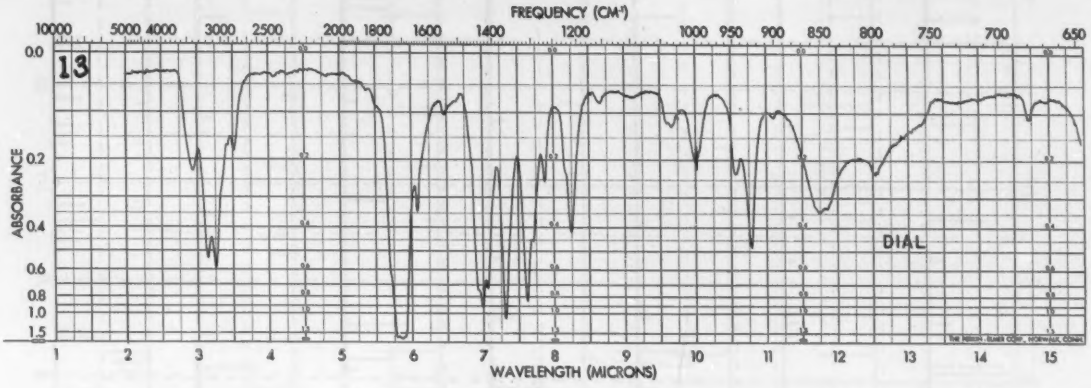


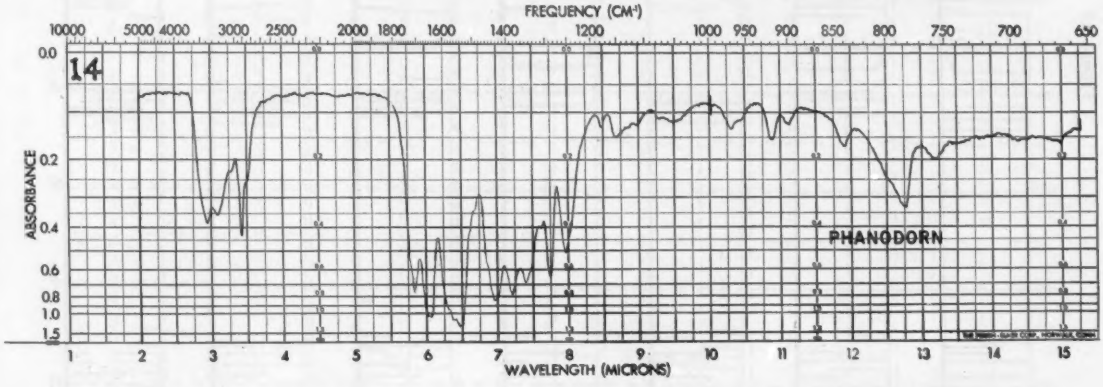
Figures 11 and 12





Figures 13 and 14





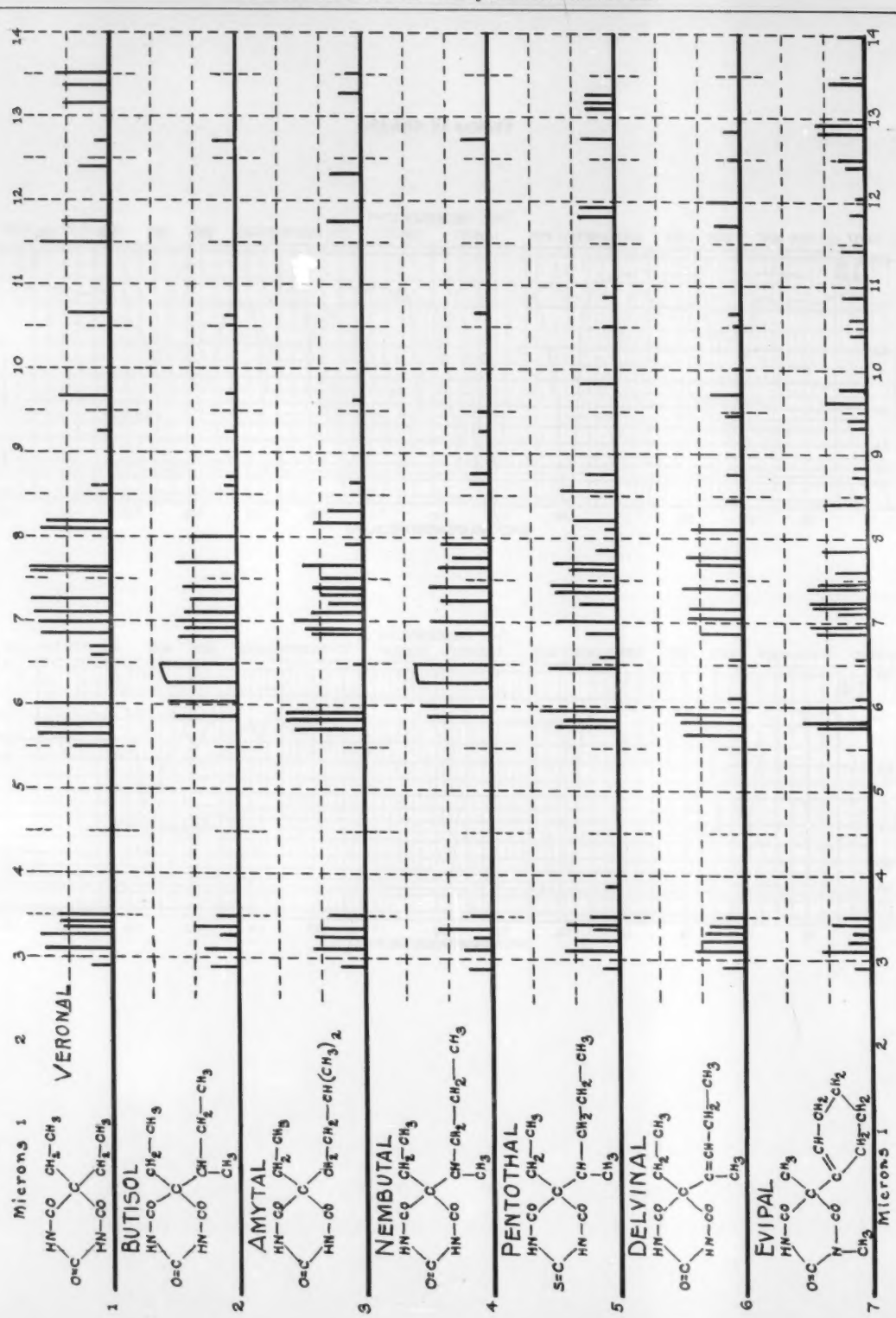

Microns 1 2 3 4 5 6 7 8 9 10 11 12 13 14
VERONAL
BUTISOL
AMYTAL
NEMBUTAL
PENTOTHAL
DELVINAL
EVIPAL
Microns 1 2 3 4 5 6 7 8 9 10 11 12 13 14

Figure 15

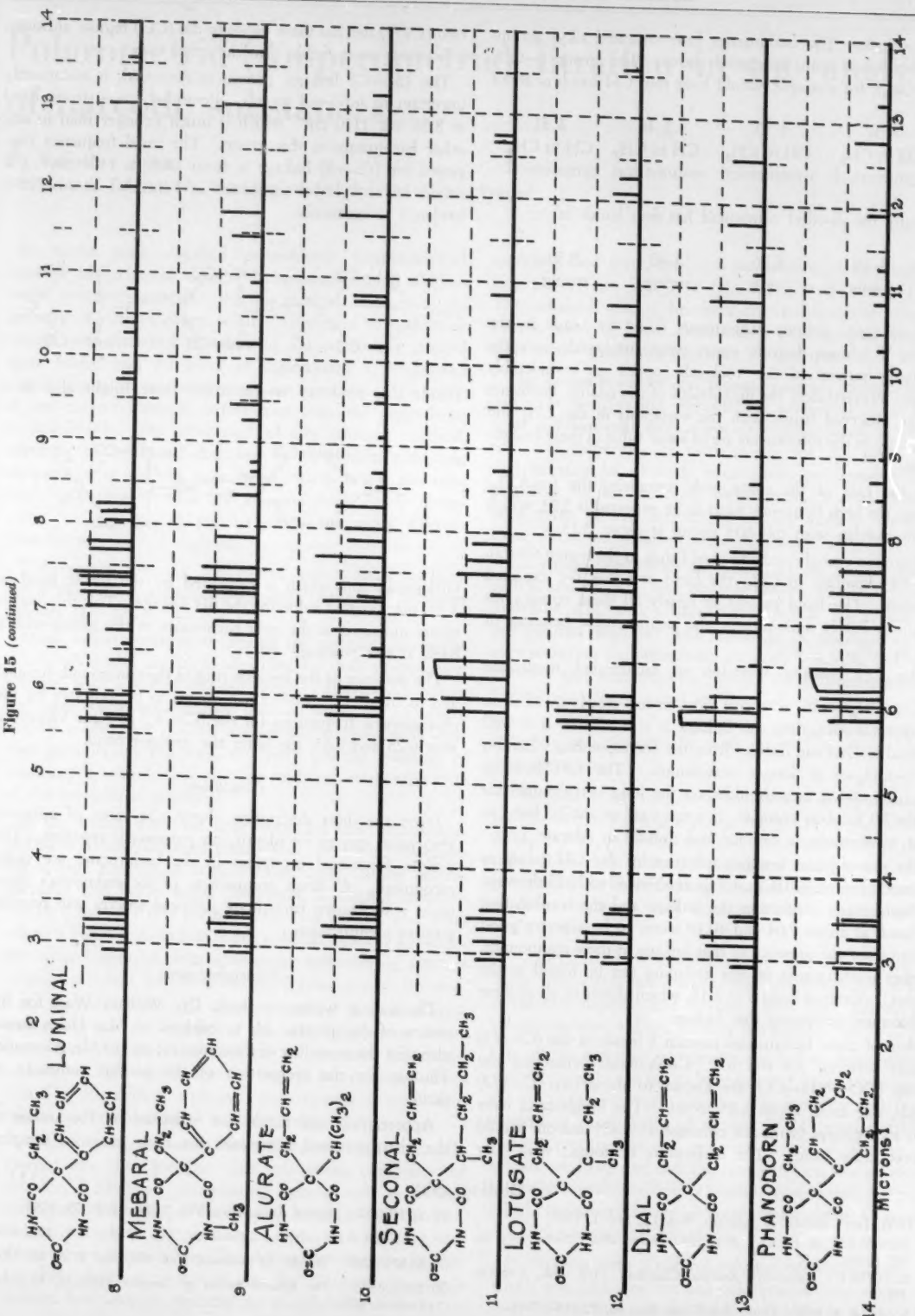


Figure 15 *(continued)*

compounds. The barbiturates have saturated alkyl groups on the carbon atom designated above. The group (—CH_2——CH_3), for example, would have four CH bands at about

3.37	3.42	3.48	3.5[1]
CH in CH_3 asymmetrical	CH in CH_2 asymmetrical	CH in CH_3 symmetrical	CH in CH_2 symmetrical

Actually the di-ethyl compound has four bands at

3.26	3.36	3.40	3.50
strong	weak	strong	strong

Perhaps more definite assignments could be made in the region if lithium flouride optics were employed, since the resolving power of the rock-salt optics is considerably lower. Nevertheless, the fluctuations of the relative intensities of the observed bands with the variations in the CH_2 and CH_3 ratio in the substituents are of some value in these asssignments.

In the case of the compounds containing the (=CH_2) group, the high frequency band to be expected is 3.23, which might overlap with the NH group at about 3.15.

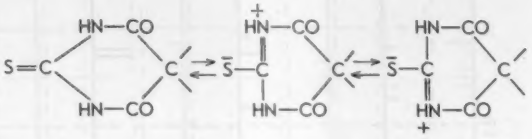
There is a complicated group of bands in the region 6.8-7.0. For CH bending in CH_2, the band at 6.8 is the expected position. The band present in nearly all these compounds at about 7.0 is undoubtedly the asymmetrical bending of CH in CH_3.

The CH bending vibration of unsaturated methylene (HC=CH_2) seems to show more or less clearly in all these compounds containing this linkage at about 7.04. It is well marked in Dial and distinct from the corresponding vibration in (—CH_2—) at longer wavelength. The CH bending vibration shows as a shoulder on the long wavelength side of the 7.0 band in Lotusate, as a mere tail of the 7.0 band to long wavelengths in Seconal and distinct in Alurate.

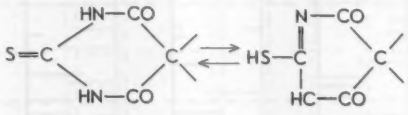
The out-of-plane bending vibration of the CH group in the methylene of (—HC=CH_2), at about 10 to 10.15 shows in all barbiturates containing the linkage and the combination of bands at about 7.04 and 10.10 seems to be a pretty good criterion for the presence of that linkage in these compounds. Further confirmation of this grouping can be found in the (C=C) vibration from 6 to 6.15, which shows in all of these barbiturates containing that linkage.

Most of these barbiturates contain 3 bands in the (C=O) region between 5.8 and 6.0. Compounds containing the group (CO—NH—CO) are known to show two (C=O) bands, one from about 5.85 to 6.0. The barbiturates have two such groups (with one common C=O) and one would expect more bands. The barbiturate Pentothal, with only two (CO's) still has three bands in the (CO) region, although it is much more feeble than the other two.

The (S=C) linkage, present in Pentothal, is notoriously uncertain in infra-red spectra. Pentothal has a strong band at 8.55 ≡ 1170 cm^{-1} which is much stronger than in any other barbiturate in this group. The usual frequency suggested for (C=S) linkage is from 1300 to 1400 cm^{-1}. It might be at a lower frequency in Pentothal because of a tendency to resonance.



Beside this tendency to resonance there might also be a



tautomerization which is suggested by the feeble band at 3.85, the accepted value for the SH linkage. This thio-barbiturate moreover is the only barbiturate in this group with a band at this position.

The presence of the benzene ring in the compounds luminal and mebaral, which contain it, seems to be indicated by the characteristic frequencies for the (C=C) in plane vibrations near 6.25 and 6.65, the latter the stronger band.

Conclusion

From the short description above, the value of infra-red absorption spectra for identifying purposes is apparent. The various functional groupings in the barbiturates are easily recognized. A direct comparison of the unknown's spectrum with known barbiturate infra-red spectra will provide positive identification.

Acknowledgement

The author wishes to thank Dr. William West for his review of the spectra. He is indebted to Miss Helen Sternglanz for the recording of these spectra; and to Mr. Alexander Thomas for the preparation of the graphic summary of them.

Appreciation and thanks are expressed by the author to the pharmaceutical companies for their generous samples.

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Polarometric (Amperometric) titration in the analysis of narcotic substances

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In recent years so-called polarometric (amperometric) titration has achieved definite recognition among electrometric titration methods. By this method, changes in the intensity of current, when suitably connected to a constant voltage, are measured in terms of the amount of control agent added and the point of equivalence is determined graphically as the intersection of lines representing the value of the current intensity before and after the equivalence is established. The advantage of this titration method, currently to be found described in all modern textbooks on quantitative analysis, is its speed and, as it is at the same time reasonably accurate and requires only simple equipment, this makes it a popular choice in many different branches of chemical analysis.

Full reports covering the use of polarometric titration also in the analysis of medical preparations have been published recently (1), (2).

Many narcotic substances (among the organic bases particularly alkaloids), are often identified by their precipitation reaction with so-called alkaloid agents. These are precisely the cases where polarometric titration offers an eminently suitable method for speedily and simply studying such addition precipitation reactions, not only for the purposes of quantitative analysis, but also for studying the composition of the precipitates produced.

In our recent work we have examined these possibilities, and have successfully used polarometric titration for analysing a large number of organic bases, using certain heteropolyacids and heavy metal complexes as control solutions (6), (7). In every case we have relied on the fact that, even where a given organic base is not polarographically apparent, the control agent is polarographically reducible — and this is quite sufficient for the purpose of polarometric titration.

As we believe that this titration method also offers wide possibilities for the control of narcotic drugs, even where these take the form of medical preparations (injections, tablets), we shall review here the organic bases thus far determined by this method, with particular reference to compounds which can be classified as narcotic drugs.

Addition precipitation reactions of organic bases are usually divided into four groups. The first group comprises the so-called " alkaline " precipitating agents, such as sodium carbonate, hydroxides of the alkaline metals, sodium acetate, sodium phosphate, potassium cyanide, sodium benzoate, etc. These agents are not basically addition precipitating agents, for their function is merely, by the alkalinization which follows their addition, to cause the precipitation of the corresponding base from, for example, alkaloid salts, usually in amorphous form and as a rule not entirely quantitatively. This method cannot be used for polarometric titration, because none of these compounds is polarographically reducible in the conditions necessary for precipitation.

The second group of precipitating reagents consists, firstly, of simple oxyacids and, secondly, of heteropolyacids. Oxyacids and their salts, such as potassium dichromate, perchloric acid and chlorates, are used mostly for the microscopic determination of alkaloids, even where polarometric determination can also be used; for example, a description has been given of the titration of certain acridine derivatives using potassium dichromate as the control solution (8).

Far greater possibilities are offered by the heteropolyacids, such as silicotungstic acid, phosphotungstic acid and phosphomolybdic acid, which have the particular merit that their precipitation reactions with alkaloids or organic bases are very sensitive; the precipitates are slightly soluble and appear instantly and quantitatively, usually in well-defined crystallized form. Such agents are especially suitable for polarometric titration, as they are compounds which are readily reducible polarographically with the use of mercury dropping electrodes.

The third group consists of solutions of heavy metal complexes, such as K_2HgI_4, K_2CdI_4, $K_2Hg(CNS)_4$, $K_2Cd(CNS)_4$, $KBiI_4$, $HAucl_4$, H_2PtCl_6 and also such substances as the so-called Reinecke's salts. These agents are also very suitable precipitants for polarometric titration and the observations made on the compounds mentioned above also apply essentially to these.

Equally favourable possibilities are offered by certain aromatic nitro-compounds and related substances such as picric, picrolonic, styphnic and flavianic acids (and, among other substances, also sodium alizarin sulfonate).

In all our titration experiments we had to determine what was the suitable voltage to be connected, taking into account the control agent used and the concentration and type of supporting electrolyte, and to find the pH most suitable for the quantitative reaction process. In the following paragraphs we have outlined the results which we obtained in the polarometric titration of organic bases (particularly alkaloids), including certain narcotic drugs, using solutions of the above-mentioned substances.

In titration with a control solution of silicotungstic acid, which was first used for the polarometric titration of nicotine (9) and nornicotine (10), we adopted, in accordance

with the polarographic behaviour of this acid, a voltage of –0.65 V (versus a calomel-saturated electrode) and obtained good results in the titration of narcotine hydrochloride, cocaine, narceine, codeine phosphate and other bases and their salts (novocaine chloride, antipyrine, amidopyrine, atropine sulfate and cinchonine sulfate), which in every case precipitated in specific proportions, quantitatively and instantaneously best of all in an acid medium (4).

A control solution of phosphotungstic acid can also be used in a similar way, adopting a voltage of – 0.4 V. We obtained good results in the titration of cocaine hydrochloride, narcotine, codeine phosphate and other compounds (antipyrine, amidopyrine, strychnine nitrate, quinine hydrochloride) (4), in approximately the same way as in the case of silicotungstic acid.

Phosphomolybdic acid is not suitable for this purpose, even where it produces a precipitate on a micro-scale with a number of organic bases and their salts; in polarometric titration the excess agent comes into contact with the mercury dropping from the electrode and produces a diminution in current intensity as a result of the reduction of molybdenum; thus the results are not readily reproducible.

Table 1 lists the identified compounds which are related to narcotic drugs and gives the most important conditions for titration with silicotungstic and phosphotungstic acid; it also states the ratio of the reaction between the base and the agent.

In all the experiments we used a volume of 10-20 ml and followed the procedure described in the following paragraphs.

With regard to control solutions of complex salts of heavy metals, we first experimented with the use of compounds of the type K_2HgI_4, K_2HgBr_4 and $K_2Hg(CNS)_4$ (6) for polarometric titration. We studied the relationship between the quantitative process of precipitation, the type of compound used in preparing the solution (HgO, $HgCl_2$, $HgBr_2$, $Hg(CNS)_2$), the quantity of anion complex-forming ingredients and the supporting electrolyte H_2SO_4, HNO_3, KI); we chose cinchonine and narcotine as standard substances for checking the reactions. We found that the titration process and the structure of the precipitate are powerfully influenced by all the above-mentioned factors, but that it is nevertheless possible to find conditions under which reproducible results can be obtained.

Table 1

Control solution and substance determined	Ratio in mole of titration agent to substance determined	Titration medium	Quantities determined (in mg)
0.01 M *silicotungstic:*			
Cocaine hydrochloride	1 : 4	0.3 N HCl	30–100
Codeine phosphate	1 : 4	0.5 N HCl	40–100
Narceine	1 : 5	0.3 N HCl	20–50
Narcotine hydrochloride ...	1 : 5	0.1 N HCl	20–50
0.01 M *phosphotungstic acid:*			
Cocaine hydrochloride	1 : 4	0.25 HCl	5–20
Codeine phosphate	1 : 4	0.25 N HCl	20–40
Papaverine hydrochloride ..	1 : 4	0.25 N HCl	30–40
Narcotine hydrochloride ...	1 : 4	0.25 N HCl	40–50

In our work we used a voltage of – 0.9 V, with a volume of about 20 ml and with 20-200 mg doses of the sample; we found 0.1 M KNO_3 or 0.1 H_2SO_4 satisfactory as the supporting electrolyte. Details are given in the original report (6). We found the best solution for titrating narcotine hydrochloride to be 0.05 M K_2HgI_4, prepared from mercuric chloride and potassium iodide in the ratio of $HgCl_2$: KI = 1 : 12, or a solution of 0.05 M K_2HgBr_4 prepared from mercuric chloride and potassium bromide ($HgCl_2$: KBr = 1/12) or from mercuric bromide and potassium bromide $HgBr_2$: KBr = 1/20 to 1/40); in each case two molecules of base reacted with one molecule of agent. We found the solution $K_2Hg(CNS)_4$, prepared differently, to be unsuitable for polarometric titration.

In the same way we studied the possibility of using the solutions K_2Cdi_4, K_2CdBr_4, $K_2Cd(CNS)_4$ and $KBiBr_4$, and found that the process of precipitation and the composition of the precipitate were influenced by the same factors as in the case of complex salts of mercury. We also found that the complex salts of cadmium and bismuth containing a sufficient quantity of bromide as an ingredient of the complex (in the case of cadmium and rhodanide), used as control agents in aqueous solutions, are more stable than analogous iodine compounds; however, as the iodine ingredient has a favourable effect in suppressing the solubility of the precipitate, we carried out titration with a control solution containing a bromide complex ingredient, but chose an iodide solution as the supporting electrolyte (volume about 20-30 ml) and so produced the solution K_2CdI_4 or $KBiI_4$ " as required ".

We obtained good results in the titration of cinchonine, codeine and narcotine hydrochloride, ethylmorphine, atropine, papaverine, strychnine nitrate, pilocarpine hydrochloride, and arecoline hydrobromide (7).

Table 2 shows the technical conditions for the titration of certain compounds which may be met with in the analysis of narcotic drugs.

We did not find complex salts of antimony suitable for these purposes.

We also studied the possibility of precipitate titration of organic bases with a control solution of Reinecke's salt (6) — $[Cr(CNS)_4(NH_3)_2]NH_4$ — which, as is known, forms highly insoluble products of addition with similar substances.

We applied a voltage of –1.1 to –1.2 V, which we established by tentative polarographic experimentation, and carried out titration in solutions of O.1 M H_2SO_4. We used a 0.04 M Reinecke's solution, which must always be prepared as needed, since these solutions lose their precipitating capacity with age. Using a volume of about 20 ml and quantities of 20 to 50 mg of the sample, we obtained good results in titrating arecoline hydrobromide (1 : 2), atropine sulfate (1 : 1), cinchonine (1 : 3), strychnine nitrate (2 : 1), ethylmorphine hydrochloride (1 : 2) and codeine (1 : 1); the molecular ratio in the precipitate between the agent and the base is given in parentheses.

The last group of substances, which gave good results when used as control agents, consists of certain aromatic nitro-compounds. Their advantages lies in the fact that,

Table 2

Titration agent	Ratio of metal and complex-forming compounds in titration agent	Substance determined	Ratio in mole of titration agent to substance determined	Titration medium	Applied voltage	Quantities determined (in mg)
0.1 M K_2CdI_4	1 : 4 to 1 : 24	Narcotine hydrochloride	1 : 2	0.1 M KNO_3	— 1.1 V	80–150
		Codeine hydrochloride	1 : 2	0.1 M KNO_3	— 1.1 V	80–200
0.1 M K_2CdBr_4	1 : 10	Narcotine hydrochloride	1 : 2	2.5% KI	— 1.1 V	100–200
		Codeine hydrochloride	1 : 2	2.5% KI	— 1.1 V	50–200
0.1 M $K_2Cd(CNS)_4$	1 : 10	Narcotine hydrochloride	1 : 2	0.1 M KNO_3	— 1.1 V	100–180
		Papaverine hydrochloride	1 : 2	0.1 M KNO_3	— 1.1 V	80–180
		Codeine hydrochloride	1 : 2	2.5% KI	— 1.1 V	80–200
0.1 M $KBiI_4$	1 : 16	Ethylmorfine hydrochloride	1 : 1	0.1 M KNO_3	— 0.6 V	80–250
		Codeine hydrochloride	1 : 1	0.1 M H_2SO_4	— 0.6 V	80–280
		Papaverine hydrochloride	1 : 1	0.1 M KNO_3	— 0.6 V	100–300
0.1 M $KBiBr_4$	1 : 16	Papaverine hydrochloride	1 : 2	0.1 M H_2SO_4	— 0.7 V	100–200
		Narcotine hydrochloride	1 : 2	0.1 M KNO_3	— 0.7 V	80–250
0.05 M K_2HgI_4	1 : 12	Narcotine hydrochloride	1 : 2	0.1 M KNO_3	— 0.9 V	20–200
0.05 M K_2HgBr_4	1 : 12	Narcotine hydrochloride	1 : 2	0.1 M KNO_3	— 0.9 V	20–200

owing to the presence of nitro-groups, they are readily reducible at the mercury dropping electrode; this makes them particularly useful for polarometric titration. Their precipitating capacity varies with the different organic bases, and, as some of our experiments show, this permits of a certain selectivity in titration of this kind.

We experimented with the use of picric, picrolonic, styphnic and flavianic acids (3), (11) and, in addition to these nitro-compounds, sodium alizarin sulfonate (which is, of course a different kind of substance) as control agents for the polarometric titration of organic bases.

Of the compounds which we tried, the most satisfactory in the titration of papaverine hydrochloride, strychnine nitrate and cinchonine was picric acid. We used a voltage of – 0.4 V. (Under these conditions, salts of cocaine, codeine and atropine, for example, did not precipitate.) Picrolonic, styphnic or flavianic acids did not give very good results, because they require buffered solutions; they are, however, in principle for the polarometric titration of organic bases, and we shall test them in some of our future experiments (for titration with picrolonic acid the voltage should be – 0.8 V or – 1.36 V; with styphnic acid, – 0.32 V; in titrating with flavianic acid, which gives good results with cinchonine and quinine hydrochloride, we found a voltage of – 1.2 V to be suitable).

In our experiments we found a solution of sodium alizarin sulphonate to be suitable for the titration of papaverine hydrochloride, narcotine, quinine, cinchonine and strychnine nitrate in buffered solutions at pH 4-6, containing 0.3 N KCl as a supporting electrolyte and with a voltage of – 0.65 V.

Table 3

Control solution and substance determined	Ratio in mole of titration agent to substance determined	Titration medium	Quantities determined (in mg)
0.01 M *Picric acid:*			
Papaverine hydrochloride...	1 : 1	pH 4.6–7	5–50
0.01 M *Sodium alizarin sulphonate:*			
Papaverine hydrochloride...	1 : 1	0.6 N KCl	10–20
Narcotine hydrochloride ...	1 : 1	0.3 N KCl	20–40

We determined the proper voltage by checking the polarographic behaviour of the compounds in question, which usually show several polarographic wave-lengths (according to the pH of the solution), only some of which are suitable for polarometric titration. Table 3 lists compounds of the narcotics series which can be titrated in this manner.

In all our polarometric titration experiments we used apparatus provided with a dropping mercury electrode for the cathode and a saturated calomel electrode for the anode, connected with the titration liquid by a salt bridge filled with a 15% solution of potassium nitrate. The necessary voltage was provided by means of a Kohlbrausch coil with a 2-volt battery. We used a galvanometer with a polarograph for measuring the intensity of the current, and an electromagnetic stirrer for mixing the liquid.

We generally carried out the titrations in the following manner (described here in summary form only; some details are given in the works cited in the bibliography appended to this report). A quantity of the sample corresponding to approximately 10-20 ml 0.01 M of a solution of an organic base or its salt is placed in a small titration vessel (suitable weights are given in the tables) and the titration medium is prepared by adding acid, buffer or supporting electrolyte as indicated for the various specific compounds. In order to support the formation of precipitate we recommend working with a small volume — about 20 ml. If necessary, a few drops of gelatine or other surface-active substance are added as a maximum suppressor — a common practice in polarometric titration. Titration then proceeds as usual in polarometric titration; i.e., after each addition of control agent (usually 0.01 M) the titrated liquid is thoroughly mixed, the precipitate formed is allowed to settle and the figure showing the intensity of the current is noted. It is usually possible to read off this figure after mixing only briefly, since the precipitation of the base with the control agent

occurs practically instantaneously (especially if a substance such as silicotungstic acid is used); but, if a substance such as picric acid is used, it is better to mix the titrated liquid several times and wait until the intensity of current remains steady. Since, in the titrations described, what appears polarographically is only the titration agent and not the precipitated organic base or its salts, the practical values of the intensity of the current do not change until the point of equivalence is reached; only after that point is there a rise in the linearly diffuse current of the excess control agent and therefore also in the value of the current; thus, the graphic representation of the titration process consists of two lines in the form of a reversed letter L, corresponding to the values of the current intensity before and after equivalence, which intersect at equivalence.

It is apparent from the foregoing that polarometric titration, the merits of which, as one of the electrometric titration methods, are well known so far as rapidity of procedure and simplicity of apparatus are concerned, may be useful also for analysing those narcotics which have the character of organic bases or their salts, particularly if use is made, as titration agents, of the compounds known as "alkaloid reagents", which, in an addition reaction with those substances, form precipitates that are highly insoluble and, under suitable conditions, have a well-defined structure.

This type of titration may be important in two ways. Firstly, it provides a very quick and reliable means of examining the structure of the precipitates that are formed — a possibility which may be useful in theoretical studies of addition reactions between organic bases and precipitating agents. Secondly, it is of practical importance in that it provides a simple means for the determination of certain narcotics. We were not particularly concerned with narcotics in our studies of the precipitation reactions of organic bases; we merely draw attention here to the possible use of the method, as we believe it can be extensively used in this field. It is highly probable that, just as suitable conditions were found for titrating the compounds mentioned in this report, it would be very easy, by analogy (possibly by slightly changing, say, the medium and the weights) to undertake the titration of other similar substances. Our experiments so far indicate that silicotungstic acid and picric acid offer in this respect the best possibilities as titration agents. Both these compounds are readily available in laboratories, and their factor can easily be determined visually by titration with a hydroxide control solution. Particular attention should be drawn to the universal utilization of silicotungstic acid, which, of all the known alkaloid reagents, forms the least soluble precipitates with organic bases. Consequently, it can be used on a micro scale; also it requires very simple titration media, as the quantitative reaction, with well-defined reaction products, is usually obtained by titration in a weak acid medium of hydrochloric acid (0.05 to 0.5 N HCl).

It may be that this universal quality of silicotungstic acid (and possibly of other precipitating agents) is in a way a disadvantage, because it does not allow sufficient selectivity in titration. If we bear in mind, however, the cases in which polarometric titration of this kind can be applied, it is obvious that this disadvantage will not arise, since in the control of narcotic drugs, whether as a basic substance or as a medicament (injections, drops, tablets), single compounds rather than mixtures will be encountered as a rule. In Czechoslovakia, for example, this titration method is used in the State Institute for Control of Medicaments with very good results for analysing commercial products and various medicaments with the character of organic bases; polarometric titration is particularly useful in checking the active substances in tablets, as there is no need to isolate the compound first by breaking the tablet down into its ingredients : all that is necessary is to dissolve the tablet in water or a weak acid medium and then titrate.

The purpose of this report was merely to draw attention in general terms to the possibility of using polarometric titration in the analysis of narcotic substances having the character of organic bases; we believe that in future this simple electrometric titration method will find widespread application in this field also.

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Professor P. O. Wolff

On 16 November 1957, Professor P. O. Wolff died in Geneva.

Professor Wolff was a well-known figure in the field of international control of narcotic drugs through his studies of drug addiction and his work as chief of the Addiction-producing Drugs Section of the World Health Organization.

Born in Berlin in 1894, he studied at the university there and obtained degrees as Doctor of Medicine and Doctor of Philosophy. He specialized in pharmacology, and one of his main interests was the study of drug addiction and drug addicts. He became a *privat-docent* at the University of Berlin. In 1931 he participated as an expert in the Geneva Conference for the limitation of the manufacture of narcotic drugs.

At the time when the national socialist regime came to power in Germany, Professor Wolff decided to go into exile. He came to Geneva and was for many years a regular contributor to the *Journal suisse de Médecine*. At the same time he carried out missions and wrote several studies for the League of Nations, and for several governments — in particular the Government of the United States of America.

In 1939 Professor Wolff went to Argentina on a mission for the League of Nations. He remained in that country until 1948 and worked there in constant liaison with the Argentine health authorities and a number of scientific bodies.

In 1949 he returned to Geneva and entered the World Health Organization, where, until he retired in 1954, he was the chief of the Addiction-producing Drugs Section.

After he retired, Professor Wolff continued his scientific activities, giving numerous lectures and writing scientific articles, as well as participating actively in the work of several international congresses. Towards the end of his life he became honorary professor in the faculty of pharmacology of Berlin's Free University.

Professor Wolff was in the full sense of the word a scholar. He wrote, in four languages, a great number of articles on many subjects, in particular cannabis, the coca leaf, opium and drug addiction in general, and it can be said that he made a significant contribution to the development of international control of narcotic drugs. At the end of his life he started a comprehensive study of synthetic narcotic drugs and wrote on that subject several authoritative papers.

It was characteristic that his scientific pursuits, though they led to great achievement, were not his only fulfilment. Throughout his life he never stopped being interested in many other aspects of human endeavour and culture. During his numerous travels he collected works of art which were amongst the treasured companions of his last years.

Professor Wolff had fought in the first world war as an officer in the German army and he had been gassed. For years he was a sick man and knew his fate, but he suffered without flinching. Up to his very last day he was working on scientific material he had written, and those who saw him at the last can say that he was a man who never gave up.

The editors of the *Bulletin* wish to extend their heartfelt condolences to his family.

Professor Axel Jermstad

On 4 November 1957, Professor Jermstad died in Oslo.

Professor Jermstad was a well-known figure in the field of pharmacology and in particular of the analysis of the alkaloids of opium.

Born on 19 May 1880, he began a course of studies at the University of Oslo but went abroad very early in life and acquired the broad outlook and wide knowledge of men and cultures which was to be one of the characteristic traits of his personality. In Switzerland, he received his degree of Doctor in Philosophy in 1920 for his thesis entitled : " Monographie und Kritik der Methoden zur Bestimmung des Morphins im Opium ", a work which later proved to be a milestone in opium research. He then travelled and studied in Germany. He had the true scientist's spirit and was never content with what he had achieved : he went to France to round out his already wide knowledge of pharmacognosy and organic chemistry and, in 1927, he received a degree of Doctor in Pharmacy at Strasbourg. He then went back to his native Norway and was entrusted with a chair at the University of Oslo. In 1932 he was nominated Dean of the Institute of Pharmacy, a post he held until 1948.

He published numerous valuable publications in the field of opium and in 1954 he was chosen to participate in the expert committee appointed by the Secretary-General of the United Nations, in pursuance of a resolution of the Economic and Social Council, to evaluate the work already done in developing and testing methods to establish the geographical origin of opium by chemical and physical means. Professor Jermstad was already collaborating in the programme established by the United Nations to develop such methods. As chairman of this committee, Professor Jermstad made a significant contribution to the work of the United Nations in the field of the international control of narcotic drugs.

Member or honorary member of a number of scientific associations around the world, Professor Jarmstad was a man of high professional status and of broad culture as well. All the people who have known him remember him not only as a scholar, but also as an upright and outspoken man, the best of colleagues and the truest of friends.

Legal trade in narcotics

The Report of the Permanent Central Opium Board[1] to the Economic and Social Council on its work during 1957[2] is on the agenda of both the thirteenth session of the Commission on Narcotic Drugs and the twenty-sixth session of the Council. This report presents an over-all picture, for the years 1952 to 1956, with special emphasis on 1956, of the legal trade in narcotics throughout the world, as it is shown by the analysis of the statistics submitted to the Board by governments, in pursuance of the international conventions of 19 February 1925 and 13 July 1931, and of the Protocol of 19 November 1948. Extracts of the report of the Permanent Central Opium Board follow.

Trends in the Licit Movement of Narcotic Drugs

Raw Materials

(a) *Opium*

World licit opium production amounted to about 775 tons in 1956. Opium-poppy cultivation was banned in Iran in 1955, so that in 1956 there were only three countries which licitly produced opium in large quantities — India, Turkey and the USSR. Their production in that year was 348 tons, 277 tons, and 105 tons respectively — i.e., 730 tons in all, or nine-tenths of the licit world production. Production declared by other countries in 1956 is divided as follows : 28 tons in Yugoslavia, 12 tons in Afghanistan, 2 tons in Japan and 1 ton in Bulgaria — i.e., 43 tons in all. Pakistan also produces a small quantity of opium, averaging 2.5 tons a year from 1952 to 1955, but has not yet supplied statistics for 1956.

During the period 1952-1956, production was highest in 1953 (1,295 tons); since then it has remained between 773 tons and 821 tons. The maximum and minimum figures for the principal producing countries are as follows : India, 629 tons in 1953 and 348 tons in 1956; Turkey, 466 tons in 1952 and 71 tons in 1954; Iran, 227 tons in 1953 and nil in 1956; USSR, 92 tons in 1953 and 109 tons in 1955. The production in other countries is too small for its fluctuations to influence the trend of world production. In considering these figures it should be remembered that weather conditions may give rise to wide variations from year to year.

Opium has three different licit uses : first, medical purposes; more than 90 per cent of quantities used in this way go into the manufacture of morphine (which is in turn almost all converted into codeine), and the rest into the compounding of medicinal preparations; secondly, quasi-medical purposes (ingestion of opium); and thirdly, exclusively non-medical purposes, in the form of prepared (smoking) opium. It is hardly necessary to add that much opium is also smoked illicitly, and the quantity used in this way cannot even be conjectured.

During the period 1952-1956, the increase in medical requirements was offset by a reduction in licit use for quasi-medical and non-medical purposes, so that the total of licit requirements taken together was nearly the same in 1956 as in 1952. India has the highest licit quasi-medical and non-medical consumption in absolute figures. The quantity so consumed, however, is diminishing year by year as a result of the Government's decision that such consumption should cease by 1959, and from 131 tons in 1952 it fell to 42 tons in 1956. Consumption of the same nature, involving some 15 tons a year, also exists in Pakistan and shows no sign of decreasing. In 1956, the exclusively non-medical licit consumption of opium (opium smoking) continued only in Thailand, where it accounted for 17 tons, and in Laos, where it amounted to a few score kilogrammes.

Reduced as far as possible to a common ratio of opium consistency, the figures of production and utilization show that in 1952 and 1953 world production was in excess of requirements, while it fell short in the three following years. Nevertheless, stocks, which stood at 1,240 tons at the beginning of 1952, had reached about 1,350 tons at the end of 1956, and this quantity alone would suffice to meet world requirements for nearly two years.

(b) *Poppy Straw*

The data which the conventions require governments to supply to the Board regarding poppy straw refer only to the quantity utilized for the manufacture of morphine and to the quantity of morphine thus produced.

The total quantity of morphine manufactured by this process was on the increase until 1953, when it reached a peak figure of 19.5 tons. Since then it has diminished, and in 1956 amounted to only 12.8 tons. That is to say, in 1953, it represented 26.4 per cent of world manufacture of morphine whereas in 1956 the proportion was only 14.7 per cent. Since 1953 there has been no reduction in the number of countries using this process, but on the whole, and especially in Hungary and the Federal Republic of Germany, less poppy straw has been used in this way. The yield also is diminishing : it averaged 2 kg of morphine per thousand kilogrammes of straw in 1953, as against only 1.5 kg in 1956.

(c) *Coca Leaves*

In the whole history of the Board it has only once been possible to arrive even at a broad estimate of licit world production of coca leaves. This was in 1954, when the figure was put at 13,113 tons. Even this estimate does not include the quantities harvested in certain South American countries where the leaves are used exclusively for non-medical purposes.

[1] Document E/OB/13, November 1957.

[2] For the report of the Permanent Central Opium Board on its work in 1951, see *Bulletin on Narcotics*, vol. IV, No. 2; for the report on 1952, see *idem*, vol. V, No. 1; for the report on 1953, see *idem*, vol. VI, No. 1; for the report on 1954, see *idem*, vol. VII, No. 1; for the report on 1955, see *idem*, vol. VIII, No. 1; for the report on 1956, see *idem*, vol. IX, No. 1.

For 1956, three countries declared their licit coca-leaf production : Peru (9,689 tons), Colombia (150 tons) and Indonesia (18 tons). Bolivia reported its production in 1954 only — viz. 3,000 tons — at which figure it would assume second place among producers. The information at the disposal of the Board is thus altogether insufficient to enable it to distinguish world production trends. This can only be done in respect of the three countries which have regulary declared their crop : Peru, Colombia and Indonesia.

In 1955, production in Peru reached 9,956 tons, the highest figure which this country has ever declared to the Board; in 1956 it declined to 9,689 tons, which was the level of production in 1952. In Colombia, production is clearly falling, dropping from 198 tons in 1952 to 150 tons in 1956. Production in Indonesia, after increasing to 26 tons in 1954, declined in the following years, but the figure for 1956 (18 tons) remains very close to that declared for 1952.

According to information supplied by the governments of four of the countries where the habit of chewing the coca leaf exists, such non-medical consumption was as follows :

	1952	*1953*	*1954*	*1955*	*1956*
			(in tons)		
Peru	9,427	9,134	9,250	9,319	9,452
Bolivia	?	?	2,764	?	?
Argentina	170	213	129	155	14
Colombia	125	120	110	100	80

All four countries have declared their intention of progressively eliminating this habit.

The quantities of coca leaves utilized for medical purposes — i.e., the manufacture of cocaine — which between 1952 and 1955 rose steadily from 300 to 623 tons, fell in 1956 to their 1952 level. In a previous report [a] the Board estimated that in 1954 the licit non-medical consumption of coca in the four above-mentioned countries was about twenty times as great as the world's total medical requirements. In 1956 it was thirty times as great, without even taking into account non-medical consumption in Bolivia for which the figure is unknown.

(d) *Cannabis*

In 1954 the Economic and Social Council invited governments to take steps to discontinue the medical use of cannabis, which the World Health Organization considers to be obsolete. At that time, 862 kg of cannabis were consumed for medical or quasi-medical purposes in 26 countries or non-metropolitan territories, 357 kg of which in India alone. In 1955, consumption continued in 25 countries and territories, giving a total of 825 kg, of which 284 kg were consumed in India. The figures for 1956 are still incomplete, since those of India (which is the principal consumer), Brazil and Pakistan have not yet arrived; nevertheless, the statistics at present available show that the total consumption, in absolute figures, has hardly diminished in the year, although it ceased in four countries.

[a] See *Bulletin on Narcotics*, vol. VIII, No. 1.

Manufactured Drugs

(a) *Morphine*

After showing a fall in 1953, morphine production resumed its upward curve, reaching 89 tons in 1955, the highest figure ever recorded, and retreating only slightly in 1956 to 87 tons. Requirements, however, have continued to increase; in 1956, as in 1953 and 1954, they reached a higher figure than production and the differences were made good by withdrawals from stocks.

The quantity of morphine converted into other substances grows larger every year : in 1956 it reached a total of 85 tons, as against 70 in 1952. This development was particularly marked in the United Kingdom, in Japan, in Poland, in the Federal Republic of Germany and in France. Not all countries, however, shared in it : in the United States this use of morphine has levelled off, and it is falling in Hungary, Switzerland, Italy and Spain. In 1956 the manufacture of codeine alone absorbed 89% of the total production of morphine; that of ethylmorphine and pholcodine 7% and 0.9% respectively, while that of diacetylmorphine, hydromorphone and of substances not liable to form addiction absorbed a total of 0.1%. Thus, 97% of the morphine manufactured in 1956 was converted into other substances, as against 90% in 1952.

Finally, the demand for morphine as an analgesic, which amounted to 5 tons in 1952, fell to 4 tons in 1956; it is declining in forty of the some sixty countries where the consumption of morphine for this purpose usually reaches at least 1 kg a year, the most noteworthy drop in terms of absolute figures being observed in the United States and in India.

(b) *Diacetylmorphine*

In 1956 three countries still manufactured diacetylmorphine : the United Kingdom (37 kg), Hungary (12 kg) and Belgium (11 kg). The entire Hungarian production and a quarter of the United Kingdom production went into the manufacture of nalorphine, a non-addiction-forming substance. Leaving aside quantities converted in this way, the net world production of diacetylmorphine was 39 kg in 1956, the lowest ever recorded.

Only two countries, Belgium and France, exported diacetylmorphine in 1956, but this was in small quantity : 1.1 kg in all. In 1952, when there were five countries exporting this drug, the figure was 68 kg.

Consumption in 1956 was equal to or in excess of 1 kg in ten countries : the United Kingdom (58 kg), Belgium (12 kg), Canada (6 kg), France (6 kg), Portugal (4 kg), Finland (2 kg), Argentina (1 kg), Italy (1 kg), the Netherlands (1 kg) and Romania (1 kg). India, a regular consumer (6 kg in 1955), has not yet supplied the figure for 1956. Total consumption (92 kg), and even that of manufacturing countries alone (70 kg), was thus greater than production. This trend has naturally had an effect on stocks, which were reduced from 228 kg at the end of 1955 to 167 kg at the end of 1956 (not including the stocks of India on either of these dates). Moreover, in several countries the utilization of diacetylmorphine will cease when the stocks are exhausted.

These figures show to what a considerable extent countries have followed the recommendation of the International Conference of 1931, seconded by the efforts of the World Health Organization and other international bodies, to put an end to the use of diacetylmorphine in therapy.

(c) *Codeine*

World consumption of codeine continues to increase; from 58 tons in 1952 it reached 76 tons in 1956. With a few exceptions (Cuba, Czechoslovakia, Spain, Turkey and the United States), all countries where the annual consumption is usually greater than 10 kg per million inhabitants have contributed to this increase.

Production has followed a similar trend, rising from 65 tons in 1952 to 80 tons in 1956.

(d) *Ethylmorphine*

In the period 1952-1956 the production of ethylmorphine has varied little, the minimum being in 1953 (5.1 tons) and the maximum in 1955 (5.9 tons). Consumption increased, rising from 4.8 tons in 1952 to 5.9 tons in 1956. The increase was most marked in France : from 0.8 ton in 1952 to 1.9 ton in 1956.

(e) *Other Derivatives of Opium Alkaloids*

It is not possible to distinguish trends in the consumption of these narcotic drugs, because it is spread over a large number of countries and non-metropolitan territories and in the majority of them does not reach 1 kg. On the other hand, production being concentrated in a few countries, affords a good indication of the development of the demand.

World Production

(*Kilogrammes*)

	1952	*1953*	*1954*	*1955*	*1956*
Narcotic drugs falling under Group I of the Convention of 1931 :					
Hydrocodone	533 *	704 *	741	761	1,011
Oxycodone	156 *	247 *	287	430	397
Thebacon	173	90	147	103	133
Dihydromorphine	—	—	—	31	49
Hydromorphone	100	108	113	125	20
Benzylmorphine	55	70	64	46	—
Desomorphine	2	—	—	—	—
Narcotic drugs falling under Group II of the Convention of 1931 :					
Dihydrocodeine	91 *	592	1,040	1,039	1,481
Pholcodine	**	206	526	561	861
Acetyldihydrocodeine	2	1	4	5	3

* Incomplete.
** This narcotic drug was brought under international control during 1952.

These figures permit of the following conclusions : for dihydrocodeine, pholcodine and hydrocodone, the trend is upward; the same applies to oxycodone and hydromorphone, but only until 1955, since the following year saw a reduction; the manufacture of benzylmorphine diminished from 1953 to 1955, and ceased in 1956; manufacture of thebacon underwent considerable fluctuations; desomorphine has not been manufactured since 1952. The manufacture of other drugs is too small or their introduction too recent, to enable a trend to be discerned.

(f) *Crude Cocaine*

Only Peru produces crude cocaine for export. Such production, which had ceased in 1949, recommenced in 1954. The 202 kg produced in that year were not exported, and this no doubt explains the small production in the following year (13 kg). In 1956 manufacture revived, but only 189 kg of the 730 kg produced in that year were exported. Thus at the end of 1956 Peru had a stock of 683 kg.

In other countries crude cocaine manufacture is merely an intermediate stage in the manufacture of cocaine.

(g) *Cocaine*

Cocaine consumption showed an upward curve from 1952 (1,757 kg) to 1954 (1,976 kg), then dropped until 1956 (1,722 kg).

The production and consumption curves are not parallel and they coincided in 1956. For the four years 1952 to 1955 there was over-production and several countries either established stocks or added to them, while in 1956 this trend ceased. Stocks at the end of 1956 would correspond to nearly two years' consumption.

(*h*) *Synthetic Narcotic Drugs*

Pethidine. — Pethidine consumption has been increasing from year to year, rising from 10.3 tons in 1952 to 13.5 tons in 1956. The increase was, however, most marked in 1955. Pethidine is consumed practically throughout the entire world, but the 9 tons consumed in the United States in 1956 represented two-thirds of world consumption in that year.

After some decline in 1953 the production of pethidine increased in the two following years and then remained stationary (15 tons). During the whole period from 1952 to 1956 — with the exception of 1953 — production exceeded consumption and the surplus was put into stocks. At the end of 1956 these were equal to about one year's consumption.

Normethadone. — This narcotic drug was brought under control in November 1954, but production statistics are only complete from 1956. In that year 1,571 kg were manufactured in the Federal Republic of Germany, 20 kg in Italy and 5 kg in Finland. Consumption figures are incomplete because the Federal Republic of Germany, which must be the largest consumer of this drug, has not brought it under the national control applying to narcotic drugs and has so far only declared its 1956 production. Five countries declared consumption of normethadone in 1956 : Belgium (13 kg), Australia (4 kg), the Netherlands (2 kg), Switzerland (2 kg) and Finland (1 kg). Brazil, which imports the drug, has not yet declared its consumption.

Methadone. — The consumption of methadone increased steadily and in 1954 reached the figure of 570 kg, the highest

ever recorded. Since then it has been falling, to 539 kg in 1955 and 450 kg in 1956.

Production and consumption figures show parallel trends. Taken as a whole, production during the period 1952-1956 fell short of consumption, with the result that the stocks decreased from 1,140 kg at the beginning of 1952 to 873 kg at the end of 1956. The latter figure, however, still corresponds to two years' consumption at the present rate.

Ketobemidone. — In 1956 eight countries (five in 1952) consumed 1 kg or more of ketobemidone : the Federal Republic of Germany (21 kg), Denmark (19 kg), Sweden (10 kg), Italy (4 kg), Norway (4 kg), Switzerland (4 kg), Belgium (2 kg) and Finland (2 kg). In the years 1952 to 1956 world consumption was as follows :

	1952	*1953*	*1954*	*1955*	*1956*
			(Kilogrammes)		
World consumption	25 *	52 *	64	68	66
Number of countries which consumed 1 kg or more	5 *	8	10	8	8

Two countries manufactured ketobemidone, Denmark and Switzerland :

	1952	*1953*	*1954*	*1955*	*1956*
			(Kilogrammes)		
Production					
Denmark	12	35	24	40	35
Switzerland	125 **	75 **	—	—	12
TOTAL ...	137	110	24	40	47

* Incomplete.
** In terms of salts.

Phenadoxone. — In 1956 this narcotic drug was manufactured only in the United Kingdom (31 kg) and Austria (1 kg); production reached its maximum in 1951, with a total of 144 kg, fell to 38 kg in 1952 and has remained stationary since then.

For 1956 only three countries declared a consumption of 1 kg or more of this drug : the United Kingdom (23 kg), the Union of South Africa (3 kg), and Australia (1 kg) — i.e., 27 kg in all, as against 63 kg in 1952.

Others. — Apart from the five synthetic narcotic drugs dealt with above, there are another 27 under international control. As can be deduced from the following tables, none of them is yet manufactured in large quantity or consumed in many countries.

World Production

(Only narcotic drugs whose production reached 1 kg in at least one country are mentioned)

(*Kilogrammes*)

Narcotic drug (Date of placing under control)	1952	1953	1954	1955	1956
Anileridine (Dec. 1956)					187
Alphaprodine (Mar. 1951)	19	24	52	45	51
Diethylthiambutene (Dec. 1955) .					15
Levorphanol (Apr. 1951)	48	11	10	54	14
Dioxaphetyl butyrate (Dec. 1955)					5
Racemorphan (Apr. 1951)	38 *	31 *	2	—	—
Isomethadone (Mar. 1951)	—	24	—	—	—
Properidine (Nov. 1954)				11	—
Betaprodine (Mar. 1951)	2	—	—	—	—

* Incomplete.

World Consumption

(Only narcotic drugs whose consumption reached 1 kg in at least one country or territory are mentioned; the number of these countries or territories is given in parentheses)

(*Kilogrammes*)

Narcotic drug	1952	1953	1954	1955	1956
Alphaprodine	13 (1)	21 (1)	37 (2)	42 (2)	40 (2)
Levorphanol	19* (4 *)	23 * (5)	24 (5)	26 (5)	16 (4)
Anileridine					15 (1)
Properidine			7 (1)	6 (1)	9 (1)
Betaprodine	1 (1)	3 (1)	—	8 (1)	8 (1)
Diethylthiambutene ...				3 (1)	5 (1)
Dimethylthiambutene **			3 (1)	4 (1)	3 (1)
Dioxaphetyl butyrate ..					2 (1)
Dipipanone ***				1 (1)	1 (1)
Isomethadone	—	18 (1)	2 (1)	—	—

* Incomplete.
** Under control since November 1953.
*** Under control since November 1954.

New Narcotic Drugs

The Board states that since the publication of its last report [4] the following narcotic drugs and their salts have been placed under international control by virtue of the provisions of the Protocol of 1948 :

Alphameprodine (α-I-methyl-3-ethyl-4-phenyl-4-propionoxypiperidine);

Anileridine (I-[2-(p-aminophenyl)-ethyl]-4-phenylpiperidine-4-carboxylic acid ethyl ester).

Further, the same control regime has been applied provisionally to the following narcotic drug :

Dextromoramide (d-3-methyl-2, 2-diphenyl-4-morpholinobutyryl-pyrrolidine), also known as R.875 and Palfium.

These narcotic drugs fall under the control provisions laid down for the drugs of Group I, which are mentioned in article I, paragraph 2, of the 1931 Convention.

Conclusions

This being the last report to be submitted by the present members of the Board, they have assessed the application of the Conventions during their whole five-year term of office and have reached, *inter alia*, the following conclusions :

On the whole there has been a distinct improvement in the operation of the system of control. In particular, statistics have been fuller and more accurate and have been more promptly submitted. To some extent, however, the work of the Board has continued to be hampered by incompleteness or delay in arrival of the returns of some governments and by failure to reply to requests for information; and there has also regrettably been a complete or almost complete lack of co-operation on the part of a few governments.

Because of difficulties inherent in the circumstances in which they are produced, the primary narcotic substances do not

[4] See *Bulletin on Narcotics*, vol. IX, No. 1.

readily lend themselves to control by means of statistics and the system is still far from being fully effective.

On the other hand, the information supplied to the Board in regard to " manufactured " drugs was both accurate and comprehensive.

One of the effects of the controls introduced by the 1925 and 1931 Conventions has been to reduce almost to vanishing point the possibility of addicts obtaining narcotic drugs from licit sources and, while there are still great numbers of addicts throughout the world, they are now obliged to look rather to sources which are, in the main, outlawed. It has thus become possible to draw a clear distinction between licit and illicit traffic in narcotic drugs.

The value of these conventions is thus well established, despite certain weaknesses and imperfections which experience has revealed in some of their provisions. It is right to record, however, that the success which has been achieved is due primarily to the high sense of responsibility displayed by most countries in this regard, including some which are not parties to the conventions.

Estimated world requirements of narcotic drugs in 1958

In pursuance of the International Convention of 13 July 1931, the Drug Supervisory Body publishes an annual statement of estimated world requirements of narcotic drugs. This statement also includes estimates for the narcotic drugs brought under international control by virtue of the Protocol of 19 November 1948.

The *Bulletin* published, in volume VIII, No. 1, a table showing for the most important narcotic drugs what the world estimates had been from 1950 to 1956, together with the actual figures of production for these drugs from 1950 to 1954. In volume IX, No. 1, the *Bulletin* published a table showing the world estimates for the same drugs for 1957, together with the actual figures of production for them in 1955. The following table shows the world estimates for these drugs for 1958, together with the actual figures of production for them in 1956,[1] the last year for which statistics have been published by the Board. The figures on production have been taken from the *Report to the Economic and Social Council* on the work of the Permanent Central Opium Board in 1957, and the figures on estimates as well as the comments have been taken from the document *Estimated World Requirements of Narcotic Drugs in 1958* published by the Supervisory Body (document E/DSB/15, 15 December 1957).

Drug	Production in 1956 [a] (kg)	Estimated world requirements in 1958 (kg)
Morphine	87,419	110,408
Diacetylmorphine	60	98
Thebaine	2,810	3,233
Codeine	80,384	95,263
Ethylmorphine	5,489	7,674
Cocaine	1,683	2,224
Pethidine	14,505	16,034
Methadone	290	678

[a] Incomplete. Most but not all countries have furnished statistics.

In its introduction to its statement, the Supervisory Body studies the impact of new drugs on its work.

" The problem of the control of narcotic drugs, whether at the national or the international level, has widened considerably in the last decade, owing to the appearance of a number of new drugs, most of them synthetic ones. The ever-growing number of these substances did not fail to affect the Supervisory Body's work. Thus, the Statement of Estimates for 1954 contained estimates for 32 drugs (17 natural and 15 synthetic). By the time the present Statement was drawn up, this number had risen to 44 (20 natural and 24 synthetic).

" The Supervisory Body's task of examining estimates has to be performed all the year round. The original annual estimates are dealt with during a session, while most of the supplementary and revised estimates — and hardly a days goes by without some being received — are dealt with in the interval between sessions, through correspondence between the members of the Supervisory Body and the secretariat. For 1956, counting the estimates submitted for each separate drug, some 1,500 of them were dealt with during sessions, and some 800 by correspondence — i.e., more than twice the numbers recorded before the advent of synthetic drugs.

" As the number of narcotic drugs increased, this work could naturally have been expected to grow in volume. Yet it grew in complexity as well, owing to the fact that the chemical descriptions of the new drugs, and particularly the synthetics, are lengthy, complicated, and can be expressed in several different ways. The Supervisory Body, for obvious reasons, was reluctant to use trade names alone in its official documents and correspondence, so that until the World Health Organization had proposed international non-proprietary names for these drugs — hitherto a lengthy process — there was little choice but to quote their chemical descriptions."

The Supervisory Body then studies the relation between estimated and actual requirements.

" The aim of the 1931 Convention was to establish an efficient system, both national and international, for limiting the manufacture and regulating the distribution of narcotic drugs, the basis for such limitation and regulation being the world's legitimate requirements for medical and scientific purposes.* In its examination of the estimates furnished by governments, the Supervisory Body constantly referred to this criterion and took account of the statistical information received by the Permanent Central Opium Board on imports and exports, consumption, manufacture and stocks. In so doing, it has often noted that the estimates furnished by certain governments were considerably higher than the statistics for previous years seemed to warrant. The Supervisory Body has therefore found it necessary on several occasions to name the countries where this over-estimation was particularly large, and to explain that the submission of exaggerated estimates ran counter to the spirit of the 1931 Convention.

" The Supervisory Body notes with satisfaction that its earlier recommendations have been taken into account and that the tendency to over-estimate, although still marked in respect of certain drugs, is definitely receding as regards both the number of countries involved and the proportion in

[1] See above, " Legal Trade in Narcotics in 1956 ".

* Preamble to the Convention of 13 July 1931.

which their estimates proved higher than actual requirements."

Finally, from the estimates submitted from 1952 to 1957 the Supervisory Body concludes :

" (*a*) the estimates of the following nine drugs, while fluctuating from year to year during the period under review, show on the whole a fairly stable trend :

Morphine	Thebacon	Ethylmorphine
Oxycodone	Thebaine	Pholcodine
Hydrocodone	Codeine	Methadone

(*b*) the figures for hydromorphone and pethidine decreased between 1952 and 1956, a trend which ceased with the estimates for 1957;

(*c*) the figures for dihydrocodeine show an unmistakable upward trend;

(*d*) for the other drugs considered, namely diacetylmorphine, cocaine, phenadoxone and levorphanol, the trend of the estimates is clearly downwards."

World Health Organization

Expert Committee on Addiction-producing Drugs : Eighth Report *

The Expert Committee on Addiction-producing Drugs of the World Health Organization held its session in Geneva from 14-19 October 1957 and made a report which was noted by the Executive Board of the World Health Organization at its twenty-first session, held in Geneva from 14 to 31 January 1958, (resolution EB 21.R4, Official Records of the World Health Organization, *1958, 83).*

The main features of this report appear from the following extracts reproduced with minor modifications:

Report on the Twelfth Session of the Commission on Narcotic Drugs of the United Nations Economic and Social Council [1]

The Committee had its attention drawn to many points of particular interest, some of which relate directly to items in its agenda.

The " Survey of Available Information on Synthetic and other New Narcotic Drugs " [2] prepared by the United Nations Secretariat was, in the opinion of the Committee, a valuable report on the present position. It was to be noted that the comparisons between different drugs were based on usual therapeutic doses rather than on gross amounts. This gives a more precise judgement of the extent to which they are being used and hence the relative importance of their usage as one of the factors in the production of addiction.

The Committee felt that it was pertinent to point out in this connexion that the present practice with respect to the introduction of new drugs does not always adequately inform the medical profession on all points of advantages and disadvantages, including addiction liability. It should be the responsibility of all concerned in such introduction to avoid over-enthusiastic or possibly premature claims and to take every precaution to see that physicians are fully aware not only of effectiveness but also of any potential dangers. Only thus can be minimized incidents of medically produced addiction which, for example, were observed particularly initially with heroin and oxycodone, and again with pethidine and ketobemidone, and seem possible to occur with *d*-3-methyl-2,2-diphenyl-4-morpholinobutyrylpyrrolidine (R 875) or other new drugs, unless necessary precautions are taken.

The Committee was fully in accord with the continuation of the search for improved narcotic drugs but thought that any subsequent introduction of a drug of this class into general medical use should be accompanied by full information on both disadvantages and advantages.

Resolutions of the United Nations Economic and Social Council

The Committee noted the increasing interest in the Technical Assistance Programme with respect to the drug addiction problem as expressed in two resolutions [3] which placed emphasis on the treatment of drug addicts. Regional seminars, in the opinion of the Committee, would materially contribute to improving the present position.

Reports of the Permanent Central Opium Board [4] and the Drug Supervisory Body [5]

The Committee noted that the consumption of certain narcotic drugs continues to increase. In part this might be accounted for by such medical uses as were not liable to be factors in the production of addiction; for example, supplementation of anaesthesia, obstetrical analgesia, endoscopic examinations.

Morphine and its derivatives

Diacetylmorphine *(heroin)*

The Committee noted that the relatively small residuum of licit use of diacetylmorphine was tending to be further reduced, indicating that the goal of the Economic and Social Council, the Commission on Narcotic Drugs, the Permanent Central Opium Board, the Drug Supervisory Body, and the World Health Organization, with respect to the cessation of the medical use of diacetylmorphine was being more nearly approached.

In view of the wide range of potency (analgesic, antitussive and otherwise) represented by the large number of substances with morphine-like effect (whether chemically derived from morphine or of completely synthetic origin),[6] diacetylmorphine could, in the opinion of the Committee, be replaced by more than one drug with less risk to public health and the choice of a particular drug should be left to the discretion of the physician according to the circumstances in any individual case.

Nalorphine

Analgesic Properties

With reference to the goal of development of a strong but non-addicting analgesic, the Committee considered recent

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* *Wld Hlth Org. techn. Rep. Ser.*, 1958, *142*.

[1] United Nations, Economic and Social Council (1957) *Commission on Narcotic Drugs : report ... on the twelfth session ... 29 April to 31 May 1957* (mimeographed document E/3010-E/CN.7/333).

[2] United Nations, Economic and Social Council (1957), *Twenty-fourth session* (mimeographed document E/CN.7/319).

[3] United Nations, Economic and Social Council (1957) *Twenty-fourth session* (mimeographed document E/RES/667(XXIV) F and G).

[4] United Nations, Permanent Central Opium Board (1956) *Report to the Economic and Social Council on the work of the Board in 1956*, Geneva (document E/OB/12).

[5] United Nations, Drug Supervisory Body (1956), *Estimated world requirements of narcotic drugs in 1957*, Geneva (document E/DSB/14).

[6] See Eddy, N. B., Halbach, H. & Braenden, O. J. " Synthetic Substances with Morphinelike Effect. Clinical experience : Potency, Side-effects, Addiction Liability ", (1958) *Bull. Wld Hlth Org.*, in press.

observations on nalorphine of great interest and importance. The antagonism of nalorphine to various effects of morphine and substances with morphine-like effect is well established. The non-addicting character of nalorphine has also been recognized. Now it is reported that nalorphine is as effective as morphine for the relief of some types of clinical pain. Unfortunately, its general use as an analgesic is impractical because of the likelihood of the occurrence of disturbing side-effects, especially if the patient has been receiving other opiates. However, many compounds related to nalorphine (or to levallorphan) are known or could be developed, which exhibit wide differences in antagonistic and analgesic actions in experimental animals. The Committee thought that it was possible that one of these may possess such a balance of properties as to constitute a practical non-addicting analgesic.

Use for Testing Addiction

With suitable conditions as to dose and time of administration it has been demonstrated repeatedly that nalorphine (and levallorphan) will precipitate a typical abstinence syndrome when physical dependence (addiction) on morphine or other substances with morphine-like effect is present. Hence such administration might be used as a tool for the diagnosis of addiction.

The Committee was of the opinion that such use of nalorphine or other antagonist could be of practical value as an aid in detecting addiction if proper safeguards are employed. Reliance should not be placed solely upon the appearance of one element of the abstinence syndrome and results should always be checked by placebo controls.

Synthetic Substances with morphine-like effect

Synthetic substances of methadone type

d-6-Dimethylamino-4,-4-diphenyl-3-heptanone (d-methadone)

In its seventh report the Committee stated the conditions under which exemption could be recommended of an optical isomer whose antipode had been shown to have strong addiction-producing properties.[7] Such conditions required specific evidence on the absence of addiction liability and specific or strong presumptive evidence on the impracticability of racemization or conversion to the optical form having addiction liability. To this should be added the impracticability of conversion into any addiction-producing drug. Referring to the request of the Government of Sweden for exemption of *d*-methadone, the Committee was of the opinion that no satisfactory evidence had been produced of non-addicting properties of *d*-methadone and that some evidence was now available presumptive of its having addiction-producing properties. In addition it has been shown that the not too difficult chemical operations of reduction and acetylation could convert the drug into acetylmethadols, drugs of known addiction-producing properties already under international control. The Committee was of the opinion that exemption of *d*-methadone should not be granted. Therefore,

The Expert Committee on Addiction-producing Drugs

Recommends that this opinion be communicated to the Secretary-General of the United Nations.

Preparation containing 6-dimethylamino-4,4-diphenyl-3-hexanone (normethadone [8])

The Committee considered a request from the Government of Italy to have the preparation "Ticarda"[9] exempted from international control by application of article 8 of the 1925 Convention. The preparation contains normethadone, a substance which has been placed in group I of article 1, paragraph 2, of the 1931 Convention, and in the opinion of the Committee it would be possible by simple means to recover the normethadone in spite of the other medicament present. Furthermore, cases of addiction to "Ticarda" have been reported. The Committee was of the opinion that exemption should not be granted in favour of "Ticarda". Therefore,

The Expert Committee on Addiction-producing Drugs

Recommends that this opinion be communicated to the Secretary-General of the United Nations.

4-Dimethylamino-3-methyl-1,2-diphenyl-2-propionoxybutane (propoxyphene [10])

The Committee examined the request of the Government of the United States of America for reconsideration of its finding with respect to 4-dimethylamino-3-methyl-1,2-diphenyl-2-propionoxybutane (propoxyphene).[11]

In its opinion it has not been shown that propoxyphene is devoid of addiction-sustaining or addiction-producing properties, although its potentiality in these respects is substantially less than that of codeine, moreover it is desirable to keep close watch on and to restrict carefully to medical and scientific needs the manufacture of a new substance with some narcotic properties, even if strict control of such a substance at all levels may not be necessary. Inasmuch as the control provided in the 1931 Convention for drugs in group II is designed for recording and supervision of manufacture and wholesale trade without restriction on retail trade, the Committee concluded that its opinion with respect to classification and control of propoxyphene and its salts as a codeine-like substance, assimilable to the substances in group II of the 1931 Convention, is valid and should be maintained. Therefore,

The Expert Committee on Addiction-producing Drugs

Recommends that its opinion with respect to 4-dimethylamino-3-methyl-1,2-diphenyl-2-propionoxybutane (propoxyphene) and its salts be communicated to the Secretary-General of the United Nations.

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[7] *Wld Hlth Org. techn. Rep. Ser.* 1957, *116* (See *Bull. Narc.*, vol IX, No. 1).

[8] Proposed international non-proprietary name.

[9] The solution for oral application contains one per cent. normethadone and two per cent. p-oxyphenyl-methylaminopropanol; one tablet contains 7.5 mg normethadone and 10 mg p-oxyphenyl-methylaminopropanol.

[10] Proposed international non-proprietary name.

[11] *Wld Hlth Org. techn. Rep. Ser.* 1956, *102* (see *Bull. Narc.*, vol. VIII, No. 1).

3-methyl-2,2-diphenyl-4-morpholinobutyrylpyrrolidine [12]

Referring to the notifications from the Governments of Belgium, France and the Netherlands, the Committee was of the opinion that *d*-3-methyl-2,2-diphenyl-4-morpholinobutyrylpyrrolidine (dextromoramide, also known as R 875), because it (1) produces morphine-like effects, (2) will suppress abstinence phenomena of a known morphine addiction, and (3) will sustain a morphine addiction, must be considered an addiction-producing substance comparable to morphine, and that *d*-3-methyl-2,2-diphenyl-4-morpholinobutyrylpyrrolidine (dextromoramide) and its salts should fall under the regime laid down in the 1931 Convention for the drugs specified in article 1, paragraph 2, group I.

Further, the Committee was of the opinion that the principle regarding control of isomeric forms stated in its seventh report [13] should apply in the present instance. Therefore,

The Expert Committee on Addiction-producing Drugs

Recommends that its opinion with respect to *d*-3-methyl-2,2-diphenyl-4-morpholinobutyrylpyrrolidine (dextromoramide [12]) and its salts and with respect to the other isomeric forms of this substance (levomoramide [12] and racemoramide [12]) and their salts be communicated to the Secretary-General of the United Nations.

Synthetic substances of pethidine type

1-(2-Morpholinoethyl)-4-phenylpiperidine-4-carboxylic acid, ethyl ester (morpheridine [14]*)*

Referring to the notification from the Government of the United Kingdom, the Committee was of the opinion that morpheridine, because it (1) produces morphine-like effects, (2) will suppress abstinence phenomena of a known morphine addiction and (3) will sustain a morphine addiction, must be considered an addiction-producing substance comparable to morphine, and that morpheridine and its salts should fall under the regime laid down in the 1931 Convention for the drugs specified in article 1, paragraph 2, group I. Therefore,

The Expert Committee on Addiction-producing Drugs

Recommends that its opinion with respect to 1-(2-morpholinoethyl)-4-phenylpiperidine-4-carboxylic acid, ethyl ester (morpheridine) and its salts be communicated to the Secretary-General of the United Nations.

1,2,5-Trimethyl-4-phenyl-4-propionoxypiperidine (trimeperidine [14]*)*

Referring to the notification of the Government of the Union of Soviet Socialist Republics, the Committee examined the evidence submitted and was of the opinion that trimeperidine (also known as Promedol), because it produces morphine-like effects and its use has been shown to result in a significant number of cases of addiction, must be considered an addiction-producing substance comparable to morphine and that trimeperidine and its salts should fall under the regime laid down in the 1931 Convention for the drugs specified in article 1, paragraph 2, group I. Therefore,

The Expert Committee on Addiction-producing Drugs

Recommends that its opinion with respect to 1,2,5-trimethyl-4-phenyl-4-propionoxypiperidine (trimeperidine) and its salts be communicated to the Secretary-General of the United Nations.

1-[2-(2-Hydroxyethoxy)-ethyl]-4-phenylpiperidine-4-carboxylic acid, ethyl ester (etoxeridine [14]*)*

Referring to the notification of the Government of France, the Committee considered that the evidence submitted indicated that etoxeridine has morphine-like properties and that supplementary tests dealing with the question of addiction were to be made. The Committee observed the chemical and pharmacological relationship between etoxeridine and pethidine and regarded these drugs as analogues such as were referred to in its first [15] and second [16] reports. In accord with the recommendation in its first report, the Committee was of the opinion that etoxeridine and its salts should be subject to the same control as pethidine (1931 Convention, article 1, paragraph 2, group I). Therefore,

The Expert Committee on Addiction-producing Drugs

Recommends that its opinion with respect to 1-[2-(2-hydroxyethoxy)-ethyl]-4-phenylpiperidine-4-carboxylic acid, ethyl ester (etoxeridine) and its salts be communicated to the Secretary-General of the United Nations.

1-(2-Hydroxy-2-phenyl-ethyl)-4-phenylpiperidine-4-carboxylic acid, ethyl ester (oxpheneridine [17]*)*

In its sixth report [18] the Committee decided to defer its opinion with respect to oxpheneridine because the information then available was of a preliminary nature. In subsequent tests it was not possible to administer sufficiently large doses of this drug on account of its insolubility and its extremely irritating properties. In the doses applied significant addiction liability was not demonstrated. Therefore the Committee was of the opinion that at this stage oxpheneridine need not be regarded as an addiction-producing substance with morphine-like effect.

"Tranquillizing" drugs

The Committee considered further information which had become available, since its last meeting, on "tranquillizing" drugs, and noted that cases of misuse are being reported with increasing frequency. This confirmed the need for governments to keep a close watch on the position, as the Committee had indicated in its seventh report.[19]

[12] Proposed international non-proprietary names of the isomeric forms: racemoramide, dextromoramide and levomoramide.

[13] *Wld Hlth Org. techn. Rep. Ser.* 1957, *116* (see *Bull. Narc.* vol. IX, No. 1).

[14] Proposed international non-proprietary name.

[15] *Off. Rec. Wld Hlth Org.* 1949, *19*.

[16] Proposed international non-proprietary name.

[17] *Wld Hlth Org. techn. Rep. Ser.* 1950, *21*.

[18] *Wld Hlth Org. techn. Rep. Ser.* 1956, *102*. (see *Bull. Narc*, vol. VIII, No. 1).

[19] *Wld Hlth Org. techn. Rep. Ser.* 1957, *116* (see *Bull. Narc.*, vol. IX, No. 1).

Coca leaf

The Committee received a statement on the situation with respect to coca leaf chewing indicating that some amelioration may be expected. In Peru, for example, measures are being taken to restrict coca plantations and to conduct an educational programme designed to emphasize that coca leaf chewing is harmful and is not indispensable.

Animal experiments for evaluation of addiction liability

The Committee was informed of progress being made in developing procedures for evaluating addiction properties using monkeys (and dogs) as test objects. Satisfactory parallelism between the results with monkeys and with man has been reported on the basis of which a screening procedure is now available. This, in its opinion, is likely to afford, at an early stage in the development of a new product, warning of the existence of particularly disadvantageous addiction-producing properties, and to make it possible to select from a group of related compounds those with least disadvantages in this respect. Such a screening process would conserve human testing facilities for critical evaluation of substances whose entrance into clinical use is being contemplated.

The Committee recognized the progress made in this field and commended the availability of an initial screening procedure for detecting addiction liability. It was of the opinion, however, that tests in man continue to be a requisite for ultimate judgement of safety of new compounds which are to be introduced into general medical use.

Addiction information centre

With reference to the statement in its seventh report on the compilation and dissemination of information on drug addiction, the Committee was informed that a similar effort in a related field had been initiated by the National Institute of Mental Health, USA. Inasmuch as this effort contemplates an extensive collection of the literature " including pharmacological, clinical, behavioural, and experimental studies of the ataraxic, psychotomimetic, and other centrally acting drugs "[20] some duplication of material which the Committee sought to compile would be liable to occur. Tentative negotiations to establish an addiction information centre have been undertaken and, if the two services could be developed jointly, duplication of effort would be avoided.

The Committee emphasized the need for and the value of an addiction information centre and hoped that the negotiations in progress would be fruitful.

[20] *Science*, 1957, *126*, 443.

International non-proprietary names

The Committee noted that the World Health Organization had informed governments of a procedure outlined in its seventh report for speeding up suggestions for and selection of proposed international non-proprietary names. No objections were raised in the replies from governments and subsequent notifications indicated that the suggested procedure was being followed. The Committee thought that the limited experience so far was very encouraging.

Preparations exempted from international narcotics control

The Committee's attention was drawn to a recapitulatory list of exempted preparations[21] and to certain anomalies therein such as the inclusion of preparations which are today virtually obsolete. The Committee considered an improvement of the list to be desirable and hoped that a suitable programme to that end could be evolved, in which it would be glad to participate.

Proposed Single Convention on Narcotic Drugs

The Committee was informed of the progress that had been made in drafting a single convention. It was understood that the World Health Organization had been participating in the drafting and would be invited formally to comment on a completed draft. An opportunity to make observations on the parts which are pertinent to the activities of the World Health Organization would be welcomed by the Expert Committee on Addiction-producing Drugs.

[21] League of Nations, Health Organisation : Recapitulatory List of Preparations exempted from the Provisions of the 1925 International Opium Convention by Application of article 8 of that Convention (document C.114.M.54.1932.III).

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